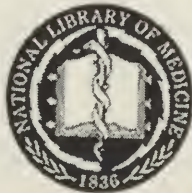


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IN THE UNIVERSITY OF MARYLAND, ETC. ETC. ETC.

"Nam quicquid essentia dignum est, id etiam scientia dignum"

PHILADELPHIA:

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TO

S. WEIR MITCHELL, M.D.,

LECTURER ON PHYSIOLOGY IN THE PHILADELPHIA MEDICAL ASSOCIATION,

AS A FRIEND, AS A SCHOLAR,

BUT, ABOVE ALL, AS ONE OF THOSE WHO HAVE LABORED MOST SUCCESSFULLY

FOR THE ADVANCEMENT OF PHYSIOLOGICAL SCIENCE;

TO WHOSE FRIENDSHIP, KNOWLEDGE, AND JUDGMENT I OWE

A GREAT PORTION OF ANY GOOD IT MAY CONTAIN,

I DEDICATE THIS VOLUME.

PREFACE.

THIS volume contains the more important Physiological Memoirs which the author has published since circumstances turned his attention to the special study of Physiology. He has yielded to the requests of several friends, in whose judgment he has confidence, and consented to their republication in their present form.

Though in so doing he is not prepared to avow an unqualified adherence to every theory he inferentially supported, he is yet unaware of any facts which controvert the conclusions arrived at from his own investigations. He has repeated, in several instances, experiments which appeared to bear different interpretations from the researches of others than those he had given to them, but has obtained no results varying essentially from those previously reached.

While he has thus been able to satisfy his own mind of the general correctness of the views expressed, it has been to him a source of much satisfaction to find them adopted by those, both in this country and in Europe, whose opinions, from the

elevated scientific position they occupy, are to him most valuable.

Most of the Memoirs appeared originally in the *American Journal of the Medical Sciences*, a journal in which it was his highest ambition to place them, and which he trusts will long continue, under the supervision of his friend, its able editor, the leading medical periodical of America. His thanks are due to its publishers for the liberality with which they have consented to this republication.

If in the collection of these Memoirs the least impetus shall be given to the cause of progressive physiology, the author will not regret their reappearance.

CONTENTS.

	PAGE
1. The Relations existing between Urea and Uric Acid.....	9
2. Urological Contributions	17
3. On the Excretion of Phosphoric Acid through the Kidneys.....	29
4. The Physiological Effects of Alcohol and Tobacco upon the Human System	43
5. Experimental Researches relative to the Nutritive Value and Phys- iological Effects of Albumen, Starch, and Gum, when singly and exclusively used as Food.....	67
6. On the Alterations induced by Intermittent Fever in the Physical and Chemical Qualities of the Urine, and on the Action of the Disulphate of Quinine	153
7. On the Injection of Urea and other Substances into the Blood.....	161
8. On the Action of Certain Vegetable Diuretics.....	173
9. Experimental Researches relative to Corroval and Vao, two New Varieties of Woorara, the South American Arrow-Poison, (with Dr. Mitchell)	181
10. On the Physical and Chemical Characteristics of Corroval and Vao, two recently discovered Varieties of Woorara, and on a New Alkaloid Constituting their Active Principle, (with Dr. Mitchell)	261
11. Experimental Researches relative to a supposed New Species of Upas.....	271
12. Further Experiments relating to the Diuretic Action of Colchicum..	296
13. Uræmic Intoxication	303

THE RELATIONS

EXISTING BETWEEN

UREA AND URIC ACID.

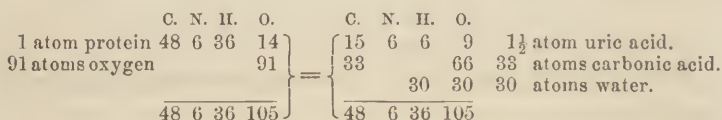
THE origin of urea is still somewhat undetermined, though numerous observations and experiments have been made by physiologists with the view of ascertaining the source or sources whence it is derived. That it is furnished, in part at least, from the metamorphosis of the effete nitrogenous tissues of the body, is beyond doubt, and is admitted by all; but that it is also derived from the oxydation in the blood of the albuminates taken as food, without their previous conversion into tissue, is not so generally received.

Liebig, Bischoff, and others hold that urea can have no other source than the metamorphosis of the worn-out tissues, and entirely reject the theory which ascribes its origin in part to the oxydation of the albuminates of the blood; while this latter view is supported by Lehmann, Frerichs, and Bidder and Schmidt, who adduce many experiments in confirmation of their opinion.

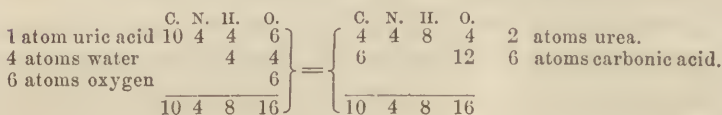
I do not intend, however, at this time, to discuss the question of the origin of urea. My object now is, to give the results of some experiments undertaken with the view of ascertaining whether the theory of Liebig, in regard to its formation from an intermediate substance (uric acid) could or could not be sustained by further investigation.

This hypothesis of Liebig, and the facts and inferences hitherto relied upon to sustain it, may be stated generally in few words. He assumes, as the groundwork of his theory, that uric acid is one of the primary products of the metamorphosis of those tissues which, being worn out, are unable to resist the chemical action of oxygen.

The following formula shows how this conversion may be effected from the oxydation of protein, a substance entering essentially into the composition of all the nitrogenous tissues:—



The uric acid thus formed is, according to Liebig, resolved, by further oxydation, into urea and carbonic acid as follows:—



According to this hypothesis, urea should be the predominant principle in the urine of all animals which lead active lives, and consequently inspire a large proportion of oxygen, more than is required for the formation of uric acid; and this latter substance, being first generated, should be converted by the surplus oxygen into urea and carbonic acid, and consequently should not be found in the urine of these animals, or, if present, should be but in small quantity.

On the other hand, in animals of sluggish habits, breathing but feebly, and consequently taking in but little oxygen, we should not expect to find urea, for uric acid would probably be the highest degree of oxydation the effete tissues or albuminates of the blood would be capable of assuming.

It also follows, from this theory, that the character of the food must exercise a very important influence in determining the formation of urea from uric acid. A non-nitrogenized diet, from containing a large proportion of carbon, should abstract oxygen in such quantity as to prevent the conversion of all the uric acid into urea, and consequently the former substance should exist in excess; while, from a highly-nitrogenized ingesta, the conversion ought to proceed under more favorable circumstances, and urea be found in greater abundance than would otherwise be the case.

Now, in fact, we find that these conditions do exist to a considerable extent. The urine of lions, tigers, dogs, etc., animals of active habits, inspiring a large quantity of oxygen, and eating highly-nitrogenized food, contains scarcely an appreciable amount of uric acid, though urea is found in abundance; and the urine of serpents, whose slothful disposition and sluggish respiration and circulation are well known, consists of little else than compounds of uric acid, no urea being present.

There are several other facts on record which tend to support the view of Liebig. Thus, Wöhler injected urate of potash into the veins of rabbits, and uniformly found an increase in the amount of urea eliminated by the kidneys. Dr. Frick has noticed that, in the convicts of the Maryland Penitentiary, uric acid was in excess in those who were allowed but little exercise, and that in the same persons the quantity of urea was proportionably diminished. In those, on the contrary, who, from the nature of their occupations, underwent more muscular exertion, he found a larger amount of urea, and a corresponding diminution of uric acid. He also found that in those to whom cod-liver oil (a substance containing a large amount of carbon) was administered, the quantity of urea was diminished in proportion to the amount of oil taken. (*On Renal Affections*, p. 113.) Dr. Frick does not state, however,

whether under this last condition the amount of uric acid was augmented or diminished.

In opposition to the hypothesis of Liebig, the experiments of Lehmann are to be taken into consideration. This eminent physiologist found, from observations made upon himself, that the uric acid was in excess at the same time with urea, and *vice versa*. Thus, while living on an animal diet, the quantity of urea daily excreted was 821·37 grains, and of uric acid 22·82 grains. On a non-nitrogenized diet, the urea amounted to 237·90 grains, and the uric acid to 11·34 grains; these substances bearing a less opposite relation to each other than should obtain, provided Liebig's theory be correct.

The fact that birds excrete no urea—their urine, like that of serpents, consisting of compounds of uric acid, while in their habits and physiology such a wide difference otherwise exists—is also opposed to Liebig's theory, and, in the present state of our knowledge, is absolutely irreconcilable with it.

Without, therefore, pretending to decide a point upon which there is so much conflicting testimony, but with the view of contributing toward its elucidation, I instituted the following experiments, the first series being performed upon myself:—

I. The object of the first experiment was to ascertain the normal quantities of urea and uric acid excreted by the kidneys in twenty-four hours, an average amount of food and exercise being taken.

I reckoned from 7 o'clock A.M., having first passed the urine which had accumulated in the night. During the day, I ate sixteen ounces of animal food, and twenty ounces of vegetable food, consisting of bread, potatoes, and turnips; drank twenty-two ounces of water, and eight ounces of strong coffee; walked two and a half miles, and rode about three miles on horseback; took no other exercise. The mean temperature for the day was 74° Fahrenheit. I passed thirty-one ounces and

two drachms of urine, of specific gravity 1.021. The total amount of urea, as determined by Liebig's method with the nitrate of mercury, from 1000 grains of the whole quantity of urine, was 682.09 grains. The total amount of uric acid, as determined from 1000 grains of the whole quantity of urine, was 13.72 grains.

These, then, may be regarded as the average normal quantities of these substances excreted by the kidneys in my own person, and as standards for the ensuing experiments.

II. The object of the second experiment was to determine the influence of exercise on the secretion of urea and uric acid, the diet being as in the first experiment.

As previously, commenced at 7 o'clock A.M. During the day, ate and drank the same articles and quantities of food as in the first experiment. Walked briskly eight and a half miles, over a hilly country; rode ten miles on horseback; pitched quoits for two and a half hours; slept six hours. Mean temperature for the day 76°. Passed thirty-four ounces and one drachm of urine, of specific gravity 1.024. Quantity of urea (determined as in the first experiment) 864.97 grains; uric acid, 8.21 grains; showing an increase in the amount of urea of 182.88 grains, and a diminution in the uric acid of 5.51 grains.

III. To determine the quantities of urea and uric acid excreted, the food and drink being the same as in the other experiments, but the body kept as nearly as possible at complete rest.

Commenced at 7 o'clock A.M. Immediately laid down on a sofa, and remained there continuously the ensuing twenty-four hours, with the exception of rising four times to urinate. Food and drink the same in every respect as before. Mean temperature for the day 73°. Slept nine and a half hours. Total amount of urine, twenty-four ounces and seven drachms. Specific gravity 1.018. Quantity of urea, 487 grains; uric acid, 24.86. A diminution of urea from the normal standard of

125.09 grains, and an increase in the quantity of uric acid of 11.14 grains.

These results may be embodied in tabular form as follows, the diet being the same in each experiment:—

	Quantity of urine.	Specific gravity.	Quantity of urea.	Quantity of uric acid.
Moderate exercise...	31 oz. 2 drms.	1.021	682.09 grs.	13.72 grs.
Increased exercise...	34 oz. 1 drn.	1.024	864.97 grs.	8.21 grs.
No exercise.....	24 oz. 7 drms.	1.018	487.00 grs.	24.86 grs.

From the above, it is, I think, conclusively shown that exercise, while it increases the amount of urea, diminishes very materially the quantity of uric acid; and that inactivity, though it diminishes the amount of urea, exercises a contrary effect upon the uric acid. As far, then, as experiments of this nature can do so, these decidedly tend to support Liebig's doctrine. It must, however, still be admitted that there are great difficulties to be overcome before this view can be regarded as actually proved.

In further reflecting upon this subject, it occurred to me that if I could, by providing a greater supply of oxygen than ordinary, induce the formation of urea in animals in which it does not naturally exist, it would almost demonstrate conclusively that the hypothesis advanced by Liebig is correct.

I therefore procured a young black-snake, (*Coluber Constrictor*), and confined it in a large jar. It was fed, *ad libitum*, on flies, grasshoppers, and other insects. At the end of a week, I examined the solid excrement which had collected in the bottom of the jar. As I expected, it contained no urea; but, on dissolving it in warm water, and adding a few drops of hydrochloric acid to the solution, a large quantity of uric acid was in a short time precipitated. I next fitted to the jar an airtight stopper, through which passed a glass tube. Through this tube I introduced, three times a day, for a week, about two hundred cubic inches of oxygen, which was retained in the

jar for two hours at a time. By its influence, the snake was rendered excessively lively; his eyes sparkled, and he darted from side to side with surprising agility. This state of activity continued during the whole time the jar remained closed. When atmospheric air was admitted, he soon relapsed into his usual sluggish state. During these experiments, his food was the same as previously mentioned, and was devoured with increased voracity.

At the end of a week, I removed the excrement from the jar, and dissolved it in warm water. A drop of the filtered solution was suffered to evaporate on a glass slide. On viewing it under the microscope, I observed most beautiful crystals of urea, mingled with those of amorphous urate of ammonia. Not being willing to rely upon the crystalline form alone as a test, I submitted the remainder of the solution to chemical examination as follows: The process employed was that recently proposed by Liebig as a modification of his method of testing for urea with the nitrate of mercury. Solutions of corrosive sublimate and bicarbonate of potash were prepared and mixed together. On adding this mixture to the solution containing the excrement of the snake, the white precipitate of urea and protoxide of mercury was immediately thrown down. This examination I regarded as showing conclusively the presence of urea, and that in no inconsiderable proportion.

From the several experiments recorded in this paper, and more especially from the last series, I consider that the theory of Liebig, accounting for the formation of urea, is probably correct. True, there are many facts difficult to account for on the supposition of its truth, and many well-founded experiments to set aside; but surely the evidence is not altogether opposed to it; and, though much still remains to be accounted for before it can be universally received, there is ground to expect that future investigations will do much toward its establishment.

UROLOGICAL CONTRIBUTIONS.

IN the *American Journal of the Medical Sciences* for January, 1855, I gave the results of experiments, instituted with the view of determining the relations existing between urea and uric acid. Those experiments showed conclusively that physical exercise augments the quantity of urea excreted, and, at the same time, diminishes the amount of uric acid; and, on the other hand, that a state of almost complete inactivity produces directly contrary effects. The investigations referred to, therefore, went to prove that, under the conditions stated, these substances, as regards quantity, stand in an opposite relation to each other, and thus supported the theory of Liebig, which ascribes the formation of urea to the continued oxydation of uric acid.

It was also demonstrated that by the respiration of oxygen in a greater state of purity than atmospheric air, urea can be formed in animals which do not ordinarily excrete it.

In the present paper I purpose giving the details of a more extended course of experiments, undertaken with the twofold object of testing the correctness of conclusions arrived at by other inquirers, and of throwing, if possible, some additional light upon the physiology of that important fluid by which the greater portion of the worn-out materials of the body is removed from the system.

The influence of mental exertion on the metamorphosis of

tissue, as exhibited in the composition of the urine, though generally admitted by physiologists, seems almost to have escaped the attention of recent investigators. If every thought emanating from the brain is to be regarded as involving the decay of a certain amount of cerebral substance, it surely becomes a question of great importance to ascertain in what manner the urine (a secretion formed essentially from the decomposition of the effete tissues of the body) is thereby affected. It has long been known that continued mental labor, and certain emotions of the mind, very materially increase the amount of phosphates eliminated by the kidneys; but, with the exception of Mosler's experiments, (referred to in the *British and Foreign Medico-Chirurgical Review*, January, 1855, p. 202,) I am not aware that any investigations have heretofore been instituted with the object of determining the effect produced upon the other constituents of the urine by psychological influences.

The experiments of Mosler, above alluded to, have very little bearing upon this point, except as regards the phosphates, which he found were regularly increased one-half by intense mental occupation. He further ascertained that, by an abundance of proteinaceous food and increased intellectual exertion, the urea and chlorine were also greatly augmented in quantity. As Lehmann has definitely shown that a full nitrogenous diet increases the amount of urea excreted, it is impossible to say how much of the effect in Mosler's experiments is to be ascribed to the intense mental occupation, and how much to the excess of protein which he had taken into his system.

In the present article, I design showing, to some extent, the effect upon the urine of increased and diminished mental exertion.

Böcker, Zobel, Julius Lehmann, and others have recently investigated the effects of tea and coffee upon the human system. These substances, forming so universally a part of the

food of man, would seem to be pointed out to him by an instinct even more powerful than reason. It is of great importance to ascertain with certainty their action upon the human economy; and any experiments calculated to enlarge our knowledge upon this point cannot but prove serviceable to the cause of medical science.

I purpose, therefore, considering in this paper the effects of tea and coffee upon the urine, and incidentally upon the system generally.

The investigations detailed are accordingly embraced under two heads:—

I. The urine, as affected by increased and diminished intellectual labor.

II. In its relations to certain articles of human consumption, tea and coffee.

As all the experiments under these heads were performed upon myself, it was easy to obtain standard amounts of the several constituents of the urine, with which to compare the results to be derived from each series of observations. I therefore reduced my food, mental labor, and physical exercise to a system, appropriating eight hours to sleep, three to bodily exercise, seven to study, and six to recreation, eating, and the performance of daily duties, requiring but little mental or physical exertion. During the twenty-four hours, I consumed sixteen ounces of fresh beef, (broiled and roasted,) twelve ounces of bread, one ounce of butter, eight ounces of potatoes, and two drachms of common salt. In the same period, I drank thirty-two ounces of water. No other food, solid or fluid, was taken into the system.

This course was, in fact, absolutely necessary to exactness, as the ordinary variations in food and exercise would very materially have influenced the results.

It may be important to state that I am twenty-seven years of

age, and at the time these experiments were commenced weighed two hundred and five pounds.

Under the several conditions of food, exercise, etc. above specified, I examined, on ten consecutive days, the total amount of urine excreted during each period of twenty-four hours, taking note of the quantity and the amount of urea, uric acid, chlorine, and phosphoric and sulphuric acids, respectively. I divided the whole quantity of urine, after accurately measuring it, into five equal parts. From one of these parts the urea was determined, and from the quantity obtained, the total amount was calculated; from another, the uric acid, and so on with each of the other constituents. The results of these analyses are given in the following table. The quantity of urine is expressed in ounces and decimals of an ounce; the weights of the several constituents are given in grains and decimals of a grain. This system is adhered to throughout.

The mean temperature of the atmosphere for the ten days of these experiments was 84° Fahrenheit.

	Quantity.	Urea.	Uric acid.	Chlorine.	Phosphoric acid.	Sulphuric acid.
1st day.....	35.60	669.10	14.90	153.37	43.27	37.12
2d day	38.32	647.45	15.55	150.43	42.52	36.15
3d day	47.75	671.06	14.16	157.08	44.74	31.10
4th day.....	36.23	691.19	14.70	155.20	43.07	38.43
5th day.....	34.17	666.22	15.23	150.58	42.64	36.45
6th day.....	36.81	668.81	14.77	154.63	43.18	38.26
7th day.....	38.06	673.90	13.51	157.17	44.50	40.60
8th day	37.29	679.16	14.04	156.11	40.00	39.05
9th day.....	37.36	672.28	14.02	150.31	48.19	36.14
10th day.....	38.00	674.09	13.58	158.16	44.56	40.41
Average...	37.95	671.32	14.44	154.29	43.66	38.47

In these and all the following experiments, the urea and chlorine were determined according to Liebig's method, with the nitrate of the protoxide of mercury; the uric acid was pre-

precipitated by hydrochloric acid; the quantity of phosphoric acid was ascertained by Liebig's and Breed's process, with test solutions of chloride of iron and acetate of soda; and the sulphuric acid, by a test solution of chloride of barium.

The foregoing table is to be regarded as exhibiting, under the conditions specified, the normal amounts in my own person, of the several constituents of the urine whose quantities were determined, and with them the results obtained in the ensuing experiments are to be compared. For, if by increasing or diminishing the amount of mental exercise or varying the diet, any change occurred in the constitution of the urine, such change would very properly be considered as resulting from this alteration—the other conditions, of course, remaining undisturbed.

Several important facts would seem to be rendered apparent from the foregoing experiments, which, however, I shall not at present stop to consider, but proceed at once to the main subjects of this paper.

I. The urine, as affected by increased and diminished intellectual labor.

A. With the view of determining the influence of *increased* intellectual exertion, I doubled the number of hours appropriated to study, taking for this purpose three hours from the number given to sleep, and four from that assigned to recreation, etc.; making a total of fourteen hours of the twenty-four, during which the mind was intensely occupied. This system I continued for ten successive days. The conditions of food and bodily exercise remained precisely as in the standard series of experiments. The urine was examined in the same manner as before. The following table exhibits the results of the analyses. The mean temperature of the atmosphere during these experiments was 82° Fahrenheit.

	Quantity.	Urea.	Uric acid.	Chlorine.	Phosphoric acid.	Sulphuric acid.
1st day.....	40.10	741.53	12.30	168.22	62.08	47.18
2d day	43.67	748.55	10.35	171.94	65.89	48.91
3d day	44.59	749.67	11.06	175.13	69.35	54.17
4th day.....	44.29	740.72	10.37	174.68	71.51	50.00
5th day.....	43.17	747.56	10.93	170.85	66.99	48.79
6th day.....	44.87	759.66	10.44	175.25	62.66	50.60
7th day.....	45.18	754.23	9.82	166.33	68.73	50.78
8th day.....	43.73	747.86	10.86	171.89	68.02	48.92
9th day.....	42.13	755.69	11.01	179.75	66.27	42.23
10th day.....	43.90	747.92	10.38	172.24	60.04	49.00
Average...	43.56	749.33	10.75	172.62	66.15	49.05

B. The influence of *diminished* mental labor was next to be ascertained. I therefore omitted studying entirely, and passed the seven hours allotted to it in the standard experiments in reading light literature, and otherwise beguiling the time in amusements requiring but little mental exertion. As previously, this was continued for ten successive days. The food, exercise, etc. remained unaltered. The effects of this course upon the urine are shown in the following table. The mean temperature of the atmosphere during this series was 77.°

	Quantity.	Urea.	Uric acid.	Chlorine.	Phosphoric acid.	Sulphuric acid.
1st day.....	33.36	590.90	14.70	144.70	28.79	37.01
2d day	33.39	581.65	15.81	148.11	25.17	37.12
3d day	30.12	591.77	15.00	143.40	28.21	39.23
4th day.....	32.86	590.13	15.88	143.52	27.46	37.00
5th day.....	32.73	586.55	17.68	141.18	25.80	35.36
6th day.....	31.00	571.36	18.73	140.25	22.75	32.71
7th day.....	35.47	583.22	18.28	139.15	23.84	35.16
8th day.....	31.33	586.65	17.83	142.30	25.82	36.80
9th day.....	31.60	570.84	19.14	140.69	20.58	33.18
10th day.....	30.59	582.43	18.27	140.17	22.60	34.62
Average...	32.24	583.55	17.12	142.34	25.10	35.81

That the results exhibited in the above tables are to be

ascribed to the increased and diminished exercise of the mind respectively, cannot, I think, be reasonably doubted. They are too well marked to admit of any other explanation, especially as the utmost care was taken that the remaining conditions of physical exercise and food should continue as in the first series of experiments.

The conclusions which are to be deduced from these investigations may be briefly stated as follows:—

1st. That increased mental exertion augments the quantity of urine.

2d. That by its influence, the urea, chlorine, and phosphoric and sulphuric acids are increased in quantity.

3d. That the uric acid, on the contrary, is very materially reduced in amount.

4th. That diminished intellectual exertion produces effects directly contrary to all the above.

Thus the brain is seen to follow the same general law which governs the other structures of the body—increased use promotes increased decay, and the products of this decay are, in like manner, removed from the system to make way for newer matter. Intense mental labor, by accelerating the metamorphosis of the cerebral tissue, necessarily requires a renewal of that tissue, and thus the nutritive elements of the food are diverted from those parts of the body by which they would ordinarily be appropriated to that organ which so imperatively demands them. The exhausting effects of long-continued study, without a corresponding increase in the quantity of nitrogenous food ingested, or the use of some one of the articles of “accessory food”—as Dr. Chambers very properly* designates them—(see *Brit. and For. Medico-Chirurgical Review*, October, 1854, p. 302,) which possesses the power of limiting the waste of tissue, scarcely admits of any other satisfactory explanation.

II. The urine, in its relations to certain articles of human consumption—tea and coffee.

A. With the object of determining the effects of *tea* upon the animal economy as evidenced in the composition of the urine, I took daily into my system thirty-two ounces of the strong infusion of black tea (sixteen ounces at breakfast, and sixteen ounces at seven o'clock in the evening) in lieu of the water forming part of the standard diet. The other food, with the physical and mental exercise, remained undisturbed. This course was continued, as in the other experiments, for ten consecutive days.

Through the influence of this substance, the mental faculties were rendered much more active, the pulse was increased in frequency, and there was a strong desire for additional bodily exercise which it was difficult to repress. At night all these phenomena were increased in intensity, and there was great indisposition to sleep. They generally lasted five or six hours after drinking the tea. About the sixth day, the physical phenomena began to subside to the natural standard, but there was still the same increased mental energy, and an inward feeling of satisfaction, which remained till the experiments were concluded. The following table exhibits the effects upon the urine; mean temperature of the atmosphere 70°.

	Quantity.	Urea.	Uric acid.	Chlorine.	Phosphoric acid.	Sulphuric acid.
1st day.....	33·35	621·73	13·05	139·07	39·15	36·25
2d day	28·40	618·50	13·00	131·81	38·49	36·17
3d day	32·61	628·55	13·02	140·63	38·71	35·90
4th day.....	35·77	619·61	13·09	130·12	37·50	35·83
5th day.....	31·03	617·11	12·60	138·43	38·25	33·18
6th day.....	30·68	607·05	11·62	148·44	40·06	30·09
7th day.....	34·14	625·09	12·41	128·54	39·55	35·45
8th day.....	26·10	617·26	13·12	136·19	37·48	31·30
9th day.....	29·84	615·38	10·36	137·78	34·85	32·03
10th day.....	29·96	606·49	12·18	130·20	36·70	28·28
Average...	31·18	617·67	12·44	136·12	38·07	33·44

Upon comparing the foregoing table with that containing the results of the first series of experiments, it is seen that the effect of substituting tea for water was to diminish the amount of urine, and with it the quantity of each of the several constituents; and this notwithstanding the additional amount of nitrogen ingested, and the increased exercise of the mind which unavoidably attended the use of tea.

These experiments are confirmatory of those of Böcker, except as regards the phosphoric and sulphuric acids, which this physiologist found were not materially affected by the use of tea, but which in the present investigations are shown to be considerably reduced in amount. The results generally are more decided than those obtained by Böcker, even though a less amount of tea was apparently ingested. This, however, may be owing to a difference in the strength of the infusions.

B. *Coffee*.—Thirty-two ounces of strong coffee, prepared by the percolation of boiling water to saturation, through the roasted grounds, were taken in the same manner as the tea, daily for ten successive days. The effects upon the brain and nervous system were even more strongly marked than when the same amount of tea was taken. They lasted about eight hours. The pulse was but slightly increased in frequency. The other functions of the body did not appear to be affected. The influence upon the urinary secretion is shown in the ensuing table. The mean temperature of the atmosphere during these experiments was 71°.

	Quantity.	Urea.	Uric acid.	Chlorine.	Phosphoric acid.	Sulphuric acid.
1st day.....	35.80	640.00	12.14	137.52	40.80	35.67
2d day	33.31	635.12	12.07	139.74	43.24	36.18
3d day	36.16	639.54	12.26	138.39	42.19	35.35
4th day.....	36.18	638.76	13.05	142.67	44.90	37.26
5th day.....	34.77	649.10	12.81	140.66	43.69	39.40
6th day.....	37.65	636.08	13.97	141.83	44.51	35.42
7th day.....	34.04	638.80	12.89	139.18	45.06	36.45
8th day.....	33.28	641.20	12.11	136.10	46.26	37.58
9th day.....	30.34	638.96	13.68	142.25	44.31	39.07
10th day.....	33.40	635.46	14.21	140.16	43.48	36.13
Average...	34.79	639.00	12.91	139.85	43.94	36.35

The above experiments show that the action of coffee upon the urine is very similar to that of tea, both diminishing the quantity of urine, and the amount of the several constituents specified in the tables, though not to the same extent. The reduction of the amount of urea is in accordance with the result obtained by Julius Lehmann, and, consequently, opposed to the opinion of Zobel, that, by the use of coffee, the quantity of this substance is increased. The effect of coffee in increasing the activity of the mind is much greater than that produced by tea.

From the above experiments with these substances, the following conclusions are deducible:—

1. That both tea and coffee are excitants of the brain and nervous system, and at the same time considerably retard the metamorphosis of the tissues.

2. That tea possesses a more powerful influence in restraining the destruction of the tissues than coffee, while this latter substance is a greater stimulant of the cerebral faculties and nervous system.

The practical application of these facts would lead to the use of tea in certain exhausting diseases, and in the laboring poor who are unable to obtain sufficient food to supply the necessary waste of animal substance, while for the rich, the student, the

literary man, the man of business—and, in fact, all others in whom it is important to keep up a certain degree of cerebral activity or physical ability, but who are not likely to suffer for want of nutriment, coffee is to be preferred.

As has been observed by Julius Lehmann, and as is also apparent from the foregoing experiments, there are two effects of coffee upon the animal economy which it is difficult to harmonize—the exciting influence upon the brain and nervous system, and the power it possesses of limiting the metamorphosis of the tissues. These effects follow the use of tea and alcohol also—and, as I have recently ascertained, tobacco—though they do not bear the same relation to each other with each of these substances.

That tea and coffee are beneficial to mankind when used in moderation, must be apparent to all who are acquainted with the recent investigations on the subject. Aside from their physical effects, the feeling of contentment they engender within us, and the disposition to reflection they encourage, are not to be disregarded in the estimation of the sum total of their good works. Sidney Smith says (*Memoirs of*, by Lady Holland:) “Thank God for tea! What would the world do without tea? I am glad I was not born before tea. I can drink any quantity when I have not tasted wine; otherwise I am haunted by blue-devils by day and dragons by night. If you want to improve your understanding, drink coffee. Sir James Mackintosh used to say he believed the difference between one man and another was produced by the quantity of coffee he drank.” When experiment demonstrates what observation has long been teaching us, it should serve to check the railings of those who can see naught but evil in the use of these and other substances which are probably nearly as serviceable.

ON THE

EXCRETION OF PHOSPHORIC ACID

BY THE KIDNEYS.

THE amount of phosphoric acid excreted through the urine has recently been specially investigated, under various physiological conditions, by Bredt,* Winter,† Mosler,‡ Bencke,§ and Böcker,|| and has also been incidentally studied by many other physiologists. Experiments relative to tissue metamorphosis are, however, always of interest, and I shall therefore offer no apology for going over, in part, the ground previously traversed by other investigators.

The experiments detailed in this paper were all performed upon myself, and had reference principally to the determination of the normal amount of phosphoric acid excreted under ordinary physiological conditions, and to the variations induced by strong bodily exercise and the internal administration of phosphate of soda. The quantity and specific gravity of the urine, and the weight of the body, were also ascertained.

The day was divided into three periods. The first, or morn-

* *Annalen der Chemie.* Band 78, Heft 2.

† *Beiträge zur Kenntniss der Urinabsonderung, bei Gesunden, Inaug. Abhandlung.* Giessen, 1852.

‡ *Beiträge zur Kenntniss der Urinabsonderung, Inaug. Abhandlung.* Giessen, 1853.

§ *Archiv für wissenschaftliche Heilkunde, B. 1, H. 4.*

|| *Archiv für wissenschaftliche Heilkunde, B. 2, H. 2.*

ing, commenced at 7 A.M., and ended at 1 P.M.; the second, or evening, extended from 1 P.M. to 10 P.M.; and the third, or night, from 10 P.M. to 7 A.M. The urine of each of these divisions was accurately measured, its specific gravity and amount of phosphoric acid ascertained, and the weight of the body, at the end of each period, carefully determined.

The methods employed were as follows:—

The *quantity* of urine was measured in a cylindrical glass vessel, holding 100 cubic centimetres, and graduated to half a cubic centimetre. For convenience, the quantity of urine is expressed in cubic centimetres instead of fluid ounces.*

The *specific gravity* was determined by means of the specific gravity bottle, and weighing in a delicate balance. The so-called urinometers sold in the United States are, according to my experience, absolutely worthless for obtaining results of even moderate accuracy.

The *amount of phosphoric acid* was ascertained by the volumetric method with perchloride of iron. As this process has not yet been fully laid before the profession in this country, it may be expedient to describe it in detail as originally proposed by Liebig and employed by Breed.†

“This process consists simply in the addition to the urine of a titrated solution of perchloride of iron, till a filtered sample of the mixture yields a blue color with ferrocyanide of potassium. It depends upon the fact that a fluid (whether neutral or acidified with acetic acid) which contains phosphoric acid gives an insoluble precipitate with a fluid containing peroxide of iron.

“The solution of perchloride of iron is best prepared by dissolving 15.556 grammes of iron in nitro-hydrochloric acid, carefully evaporating to dryness in a water-bath, so as to expel the excess of acid, and dissolving the solid residue in 2000 cubic

* Thirty-three cubic centimetres are about equal to one fluid ounce.

† Op. cit.

centimetres of water. One cubic centimetre of this solution precipitates ten milligrammes of phosphoric acid.

"Instead of such a solution of perchloride of iron, one of indefinite concentration may be employed, the strength of which has been previously ascertained by titration with a solution of phosphate of soda containing a known quantity of phosphoric acid. In each case the solution of perchloride of iron must be free from chloride of iron.

"Should the urine, whose proportion of phosphoric acid is to be determined, be of alkaline reaction through the decomposition of its urea, it is probable that a part of the phosphoric acid has already been precipitated in union with lime or magnesia. In this event it is necessary to redissolve the precipitate by the addition of a few drops of nitric acid.

"The urine is measured and well agitated. A definite quantity (100 cubic centimetres or more) is, by means of a pipette, placed in a beaker-glass, and a solution of acetate of soda (a considerable amount when nitric acid has been added) and acetic acid mixed with it. Then, by means of a burette, the perchloride of iron is added, and the urine frequently tested, to determine whether or not the whole of the phosphoric acid has been precipitated, till a trace of an excess of iron has been added. In order to ascertain when this last is the case, a piece of filtering paper, moistened with a solution of ferrocyanide of potassium, is spread out upon a white porcelain dish (or on a glass plate over white paper) and a folded piece of filtering paper pressed against it by means of a glass rod on which a drop of the urine hangs. If an excess of solution of iron has been added, a blue color appears in three or four seconds; the quantity of perchloride of iron necessarily employed is noted. In a similar manner two other portions of the urine should be proceeded with. If the results agree, it is calculated how much of the solution of iron would have been necessary for the whole

quantity of urine, and the amount of phosphoric acid indicated by this quantity of the reagent is that which the total amount of urine contains."

The acetate of soda and acetic acid may be conveniently employed by making a solution of the salt in the proportion of twenty grammes to 160 cubic centimetres of distilled water, and adding forty cubic centimetres of the concentrated acid. Ten cubic centimetres of this solution contain one gramme of acetate of soda and two grammes of acetic acid. In ordinary cases, twenty cubic centimetres are used for every 100 cubic centimetres of urine.* Where the urine is alkaline, and it has been necessary to dissolve any resulting precipitate of phosphates with nitric acid, as before specified, the quantity of the above solution to be employed should range from twenty to forty cubic centimetres, according to the amount of nitric acid necessarily added.

By the foregoing described method results are obtained of at least as great accuracy as by precipitation and subsequent weighing, and with much less expenditure of time and labor.*

The weight of the body was ascertained by means of a balance capable of turning with .01 pound when loaded with 250 pounds.

During the experiments I breakfasted at 7 A.M., lunched at 1 P.M., and dined at 5 P.M. At breakfast I ate five ounces of beef-steak, eight of bread, half an ounce of butter, and ten grains of salt, and drank six ounces of strong coffee, containing two drachms of cream and two of white sugar. At luncheon I ate three ounces of cold roast beef, six of bread, two drachms of

* The decimal system of the French is so much more convenient than our own, in chemical manipulations, and is now so generally employed in such operations, that I have not deemed it necessary to reduce the weights and measures of the foregoing process to the English standard. A little reflection, and an acquaintance with the general principles of chemistry, will enable those who wish it to perform all the described manipulations with the domestic weights and measures.

butter, and twenty grains of salt. At dinner I took six ounces of strong beef soup, eight of roast beef, four of potatoes, four of bread, two drachms of butter, and half a drachm of salt, and drank four ounces of coffee. In addition to this food I drank, at each meal, twelve ounces of water, and six immediately before going to bed.

In the twenty-four hours, therefore, I ingested sixteen ounces of beef, eighteen of bread, six of soup, four of potatoes, one of butter, one drachm of salt, two of cream, and two of sugar, and drank ten ounces of coffee and forty-two of water.

This diet does not differ greatly from that followed during former investigations of the effects of alcohol and tobacco upon the human system.*

The standard amount of physical exercise (divided as equally as possible between the morning and evening periods of the day) consisted in walking about one thousand yards.

The mental exercise consisted of reading and studying from 9 A.M. to 1 P.M., chemical investigations from 2 P.M. to 5 P.M., and reading (generally of a light character) from 8 P.M. to 10 P.M., at which latter hour I retired to bed. The remaining active hours of the day were passed in necessary duties, recreation, etc. I awoke at about 7 A.M., and consequently slept about nine hours. The feces were evacuated at a few minutes after 7 A.M., and the urine at the termination of each period.

The quantity of urine is given in cubic centimetres, the phosphoric acid in troy grains, and the weight of the body in avoirdupois pounds.

I.

STANDARD SERIES.

This series continued eight days, under the conditions already specified. The results are contained in the accompanying table :—

* American Journal of the Medical Sciences, October, 1856.

TABLE I.

DATE.	MORNING, (6 hours.)				EVENING, (9 hours.)				NIGHT, (9 hours.)				WHOLE DAY.			
	Quantity of urine.	Specific gravity.	Phosphoric acid.	Weight of body.	Quantity of urine.	Specific gravity.	Phosphoric acid.	Weight of body.	Quantity of urine.	Specific gravity.	Phosphoric acid.	Weight of body.	Quantity of urine.	Specific gravity, (mean.)	Phosphoric acid.	Weight of body, (mean.)
April 2d...	427.5	1022.51	20.978	196.50	667.8	1025.30	25.103	196.72	498.3	1024.81	14.090	196.55	1593.6	1024.20	60.171	196.55
" 3d...	441.6	1023.04	21.820	196.42	825.5	1022.17	28.251	196.59	345.7	1025.43	10.241	196.50	1612.7	1023.54	60.312	196.50
" 4th...	378.0	1024.35	17.531	196.41	594.8	1025.21	31.518	196.53	685.4	1023.62	16.356	196.44	1658.2	1024.39	65.405	196.46
" 5th...	426.7	1023.46	22.430	196.48	500.6	1024.37	25.211	196.75	524.8	1024.12	10.287	196.61	1452.1	1023.98	57.928	196.61
" 6th...	504.2	1021.59	15.260	196.30	515.4	1025.11	19.514	196.45	438.9	1024.67	15.785	196.40	1458.5	1023.79	50.559	196.38
" 7th...	450.1	1022.41	19.389	196.15	492.7	1025.04	22.301	196.27	401.5	1025.02	16.424	196.24	1344.3	1024.15	58.114	196.22
" 8th...	518.5	1021.07	24.758	195.89	486.9	1025.49	20.427	196.01	454.2	1024.35	17.438	195.94	1459.6	1023.63	62.623	195.94
" 9th...	412.4	1021.58	22.507	195.95	514.6	1024.21	25.407	196.10	489.6	1023.59	10.527	196.04	1416.6	1023.12	58.441	196.03
Average...	444.8	1022.50	20.584	196.26	574.8	1024.61	24.729	196.44	479.8	1024.45	13.893	196.34	1499.4	1023.97	59.194	196.33

An examination of the foregoing table shows the following facts :—

1st. The quantity of urine excreted was highest for the evening period, next highest during the night, and lowest in the morning.

2d. The evening urine was of highest specific gravity, the night urine somewhat less, and the morning urine the lowest.

3d. The evening urine contained the greatest amount of phosphoric acid, the morning urine the next largest, and the night urine the smallest.

4th. The weight of the body was greatest at evening, next greatest at night, and smallest in the morning.

The following table (II.), showing the amount of urine and of phosphoric acid passed per hour during each period, the proportion of phosphoric acid in 1000 c. cen. of urine, and the quantity of urine and phosphoric acid excreted for each pound weight of the body, will tend further to elucidate the subject.

From this table it is seen that hour for hour more urine and phosphoric acid were excreted during the morning period than either the evening or night, and that the proportion of this latter substance in one thousand cubic centimetres of urine was greater for the morning urine than for the urine of either of the other periods. Considering that the morning embraced but six hours, while the evening and night were each nine hours long, the former period also shows a greater excretion of urine and phosphoric acid, for each pound weight of the body. Indeed, the *absolute* average amount of phosphoric acid, in relation to the weight of the body, is much less during the night than the morning, and is but little greater during the evening, notwithstanding the difference in the number of hours.

TABLE II.

Date.	MORNING, (6 hours.)				EVENING, (9 hours.)				NIGHT, (9 hours.)				WHOLE DAY.							
	Urine per hour.	Phosphoric acid per hour.	Phosphoric acid in 1000 C.C.M. of urine.	Urine per pound weight of the body.	Urine per hour.	Phosphoric acid per hour.	Phosphoric acid in 1000 C.C.M. of urine.	Urine per pound weight of the body.	Urine per hour.	Phosphoric acid per hour.	Phosphoric acid in 1000 C.C.M. of urine.	Urine per pound weight of the body.	Urine per hour.	Phosphoric acid per hour.	Phosphoric acid in 1000 C.C.M. of urine.	Urine per pound weight of the body.	Phosphoric acid per pound weight of the body.			
April 2d...	71.2	3.466	48.67	2.12	.157	74.2	2.799	37.72	8.39	.122	55.3	1.565	28.30	2.53	.071	66.4	2.507	37.75	8.11	.306
" 3d...	73.6	3.636	49.40	2.24	.105	91.7	3.139	32.05	4.10	.143	36.2	1.138	31.16	1.75	.052	67.4	2.513	37.28	8.21	.307
" 4th...	63.0	2.921	46.36	1.95	.089	66.1	3.502	52.98	3.02	.163	76.2	1.150	15.09	3.48	.083	69.1	2.725	39.47	8.44	.338
" 5th...	71.1	3.405	47.88	2.12	.114	55.6	2.801	50.89	2.54	.128	58.3	1.143	19.60	2.66	.052	60.5	2.413	39.88	7.83	.294
" 6th...	84.0	2.543	30.27	2.55	.079	57.2	2.168	37.90	2.62	.099	48.6	1.754	36.09	2.23	.080	60.7	2.106	34.69	7.43	.252
" 7th...	75.0	3.261	43.48	2.29	.098	54.7	2.478	45.32	2.51	.113	44.6	1.825	40.91	2.55	.083	56.0	2.421	43.23	6.85	.296
" 8th...	86.4	4.109	47.55	2.69	.126	54.1	2.269	41.92	2.43	.104	50.5	1.937	38.35	2.86	.088	60.8	2.609	42.91	7.42	.312
" 9th...	68.7	3.751	54.71	2.61	.114	57.1	2.823	49.47	2.62	.129	59.9	1.169	19.34	2.44	.053	58.7	2.435	43.01	7.22	.298
Mean	74.1	3.430	46.27	2.23	.104	63.8	2.468	38.68	2.92	.113	53.3	1.543	28.95	2.44	.070	62.4	2.466	39.52	7.64	.301

It would appear from these experiments, that no definite relation exists between the weight of the body and the amount of urine and phosphoric acid excreted, and that the quantity of this latter substance eliminated bears no constant ratio to the amount of urine or to its specific gravity. The investigations are, however, far too meager to warrant the deduction of definite conclusions on any of these points.

II.

EFFECTS OF PHYSICAL EXERCISE.

The physical exercise of this series consisted in the lifting of a weight of one hundred pounds ten feet in a minute, for three periods of fifteen minutes each, at intervals of one hour. This exercise was only employed in the morning, and was in lieu of so much of the time given in the former series to study. In all other respects the course of living was the same as before stated. This series of experiments was continued for five days. The following table (III.) exhibits the results.

From the examination of this table the influence of the extra amount of physical exercise taken is very readily perceived.

1st. It is seen that in the morning period the quantity of urine, its specific gravity, and amount of phosphoric acid are very considerably increased over the normal average for this period.

2d. That in the evening there is a reduction of the amount of urine and phosphoric acid, instead of, as in the former series, an increase. The specific gravity of the urine is not so much raised as in the standard series.

3d. That at night the urine and its specific gravity fall to the minimum, while the phosphoric acid rises slightly over the evening average.

4th. That for the whole twenty-four hours, as compared with the averages for this period of the preceding series, there is an increase in the quantity of urine, a slight decline in the specific gravity, and a very considerable augmentation of the amount of phosphoric acid excreted.

TABLE III.

DATE.	MORNING, (6 hours.)				EVENING, (9 hours.)				NIGHT, (9 hours.)				WHOLE DAY.			
	Quantity of urine.	Specific gravity.	Phosphoric acid.	Weight of body.	Quantity of urine.	Specific gravity.	Phosphoric acid.	Weight of body.	Quantity of urine.	Specific gravity.	Phosphoric acid.	Weight of body.	Quantity of urine.	Specific gravity, (mean.)	Phosphoric acid.	Weight of body, (mean.)
April 10th..	623.3	1023.18	32.715	195.46	525.2	1024.25	18.534	195.40	510.5	1021.04	18.215	195.50	1659.0	1022.82	64.464	195.45
" 11th..	584.9	1024.05	30.244	195.30	604.5	1024.03	22.613	195.28	539.0	1021.98	25.124	195.38	1728.4	1023.12	77.981	195.32
" 12th..	645.7	1023.20	25.187	195.15	493.5	1025.11	12.250	195.20	478.5	1022.30	17.382	195.22	1617.7	1023.53	54.819	195.19
" 13th..	615.5	1023.54	33.250	194.90	518.0	1024.51	20.327	194.87	482.7	1022.25	20.845	195.02	1616.2	1023.43	74.422	194.93
" 14th..	580.5	1024.80	36.185	194.82	524.6	1024.15	26.450	194.74	512.6	1021.87	24.612	194.81	1617.7	1023.61	87.247	194.79
Average..	609.9	1023.75	31.516	195.12	533.1	1024.41	20.034	195.09	504.6	1021.74	21.235	195.18	1647.8	1023.30	71.786	195.13

It is also seen from this table that the weight of the body is almost invariably highest at night, next highest in the morning, and lowest in the evening.

The comparatively low average specific gravity of the urine for the whole day was doubtless due to the fact of the employment of the exercise only in the morning. The immediate effect of the physical exertion is seen to have been an increase in the density of the urine. Had the exercise been kept up during the other periods of the day, the result would undoubtedly have been an augmentation for the whole twenty-four hours.

III.

EFFECTS OF PHOSPHATE OF SODA.

During this series of investigations I took three hundred grains of crystallized phosphate of soda per day: one hundred at 9 A.M., one hundred at 3 P.M., and one hundred at 10 P.M. At each of these hours, therefore, I ingested nearly twenty grains of phosphoric acid into the system, making sixty grains in the twenty-four hours. This series lasted, as the preceding, five days. The conditions of food, exercise, etc. remained as in the first series. The results are embodied in the ensuing table (IV.)

From this table it is seen that, after the exhibition of phosphate of soda, the following effects ensued:—

1st. For the morning period, there was a considerable increase in the quantity of urine, its specific gravity, and amount of phosphoric acid, as compared with the means of the standard series.

2d. For the evening, the quantity of urine was slightly reduced, and the specific gravity and phosphoric acid augmented.

3d. For the night period, the quantity of urine was but slightly affected; the specific gravity and phosphoric acid were, however, increased.

4th. For the whole twenty-four hours, the quantity of urine, its specific gravity, and amount of phosphoric acid were all increased.

TABLE IV.

DATE.	MORNING, (6 hours.)				EVENING, (9 hours.)				NIGHT, (9 hours.)				WHOLE DAY.			
	Quantity of urine.	Specific gravity.	Phosphoric acid.	Weight of body.	Quantity of urine.	Specific gravity.	Phosphoric acid.	Weight of body.	Quantity of urine.	Specific gravity.	Phosphoric acid.	Weight of body.	Quantity of urine.	Specific gravity, (mean.)	Phosphoric acid.	Weight of body, (mean.)
April 16th..	585.6	1024.09	36.891	194.92	523.7	1025.51	40.125	194.98	429.2	1025.40	27.896	194.89	1548.5	1025.00	104.412	194.93
" 17th..	627.9	1024.11	42.587	194.83	480.5	1026.60	35.217	194.96	518.6	1025.05	29.231	194.96	1617.0	1025.25	107.035	194.91
" 18th..	685.4	1024.48	47.256	194.70	527.4	1025.38	30.625	194.81	483.6	1026.11	33.192	194.75	1696.4	1025.82	111.073	194.75
" 19th..	592.4	1023.80	39.110	194.51	500.2	1025.14	38.246	194.55	539.3	1023.04	25.451	194.53	1631.9	1023.99	102.807	194.53
" 20th..	550.5	1024.23	33.475	194.20	531.0	1025.30	36.351	194.32	490.1	1026.58	29.397	194.23	1577.6	1025.37	99.223	194.25
Average..	608.3	1024.14	39.761	194.63	512.3	1025.58	36.112	194.72	492.1	1025.23	29.033	194.67	1614.2	1024.98	104.910	194.67

The weight of the body declined steadily during each series of investigations.

Of the sixty grains of phosphoric acid daily ingested, it is probable the whole was not eliminated with the urine. Thus the average normal amount of phosphoric acid daily excreted is seen to have been 59·104 grains, while under the administration of the phosphate of soda, it rose only to an average of 104·910 grains, leaving 14·194 grains either discharged with the urine or retained in the system.

The results obtained by the foregoing investigations differ in several important points from those arrived at by the physiologists before mentioned.

The meagerness of the experiments forbids the deduction of definite conclusions from them, and they are, therefore, only submitted as contributions to a fuller understanding of the subject to which they pertain.

THE
PHYSIOLOGICAL EFFECTS
OF
ALCOHOL AND TOBACCO UPON THE HUMAN SYSTEM.

THE present paper is intended to exhibit the action of alcohol and tobacco upon the system generally, and, more especially, upon the important functions concerned in the metamorphosis of tissue.

The experiments illustrative of the effects of these substances were performed upon myself, and were conducted with all the care and accuracy which my limited facilities permitted. Those only who are familiar with investigations of this character can appreciate the time and labor necessary to conduct them properly, and but for the improved and extended system of volumetric analysis now so much employed in physiological chemistry, I should probably have been compelled to refrain from inquiries necessarily tedious at the best, but incomparably more so when the older methods of quantitative analysis are observed. Yet, when we reflect that, however tiresome and even disgusting physiological investigations often are, it is only by actual experiments we can ever hope to lay the foundations of true physiological science, we can well afford, for the sake of accomplishing so noble an end, to labor cheerfully on, even though the way be

not so nice as we might desire. The day of extravagant theories, unsupported by observation, has gone by, and he who has nothing better to offer than the unsustained creation of a dreamy mind, meets with but little attention, and merits still less than he receives.

The influence of *alcohol* upon the human system has recently been the subject of thorough investigation by Dr. Böcker, who, with a degree of zeal worthy the importance of the inquiry, performed a series of experiments upon himself which have rarely been excelled for completeness and accuracy; but as the conclusions derived from his observations have met with the opposition of several distinguished physiologists, additional investigation seemed not altogether uncalled for.

The experiments relating to the action of *tobacco*, detailed in the present paper, are believed to be the first of the character which have been performed. Physicians have heretofore been content to decri its use as uniformly injurious, without seeking for a reason for its deleterious influence, or even attempting to show that it was so generally pernicious as they believed. That both it and alcohol, when used with discretion, are capable of exercising highly beneficial effects upon the organism, will be abundantly shown from the ensuing experiments. Their influence, however, is not constantly advantageous, and when employed under circumstances which do not justify their use—like many other articles of food of much less doubtful reputation—they may produce results which are far from conducive to health.

My own system was, I conceived, well calculated to exhibit the action of these agents satisfactorily. Not being in the habit of using either of them, I was peculiarly sensitive to their influence, and was able to perceive effects which, in a person more habituated to their use, might have escaped observation.

My manner of living during the succeeding investigations was as follows:—

I arose every morning at six o'clock, and retired to bed every night at eleven. I was thus awake seventeen hours, and asleep seven. The seventeen waking hours were thus appropriated: ten were assigned to study of as uniform a character as possible, five to daily duties, recreation, etc., and two to a uniform system of physical exercise. This course was rigorously insisted on throughout the whole of the experiments with both alcohol and tobacco.

ALCOHOL.—I had three objects in view in investigating the action of this agent.

1. To observe its effects upon a system in which the weight of the body was *maintained at a nearly uniform standard* by a sufficiency of food.

2. To ascertain its influence upon an organism where the body *lost weight* from a deficiency of food.

3. To determine its action upon a system where the body *gained weight* from an excess of food.

The experiments under these heads related to the weight of the body, the quantity of carbonic acid and aqueous vapor expired in respiration, the weight of the feces, the quantity of the urine, and the amount of its free acid, urea, uric acid, chlorine, and phosphoric and sulphuric acids. Besides these special determinations, I observed minutely every circumstance connected with my general health which could reasonably be ascribed to the action of the alcohol. I regret that I had no means at my command for accurately determining the amount of the cutaneous transpiration. Wherever this was sensibly affected it is noticed, but the liability to error when judging solely from sensation must not be forgotten.

The weight of the body was taken every day at 7 A.M. and at 2 and 10 P.M. The means of these observations are given in the tables. The carbonic acid and aqueous vapor exhaled from the lungs were determined by causing the expired air to pass through a tube containing chloride of calcium, and then through a satu-

rated solution of baryta contained in two Woulfe's bottles. The excess of weight of the chloride of calcium tube indicated the amount of aqueous vapor, and from the quantity of carbonate of baryta formed, the carbonic acid was estimated. These determinations were made at 9 A.M. and at 2 and 10 P.M., and were continued one minute. From the mean of these observations the quantity for the day was calculated. As Vierordt has shown that the rate of respiration exercises a material effect upon the quantity of carbonic acid expired, I breathed during these observations uniformly fourteen times per minute, which is about the average natural frequency of my respiration. As comparative results were what I most desired, this method of estimation was sufficiently accurate.

The feces were weighed at 8 $\frac{1}{2}$ A.M., immediately after their evacuation. The whole quantity of urine passed during the twenty-four hours was accurately measured. The acidity of this fluid was determined by a test solution of ammonia, and was estimated as oxalic acid, and the urea, uric acid, chlorine, and phosphoric and sulphuric acids were ascertained as in the experiments recorded in the *American Journal of the Medical Sciences* for April, 1856.

In the following tables the weight of the body is given in pounds and decimals, the feces in ounces and decimals, and the quantity of urine in fluidounces and decimals. The weights of all the other substances are stated in grains and decimals. This system, though not so convenient as the French, has the advantage of being more commonly understood in this country, where the latter method is not yet generally adopted.

In the series of investigations previously detailed, ten days was the period fixed upon for obtaining average results. Further experience has, however, convinced me that these can be obtained of sufficient accuracy in five days, and, where so many observations have to be made, the saving of time is an item not to be disregarded.

I. The action of *alcohol* where a uniform weight of the body was preserved.

After several trials, I found that food of the quality and quantity stated below, and taken as specified, kept up my weight to a nearly perfectly fixed standard.

I breakfasted at seven, lunched at one, and dined at five. At breakfast I ate five ounces of beef-steak, eight of bread, one-half ounce of butter, and ten grains of salt, and drank six ounces of strong coffee, containing two drachms of cream and two of white sugar. At luncheon, I ate three ounces of cold roast beef, six of bread, two drachms of butter, and twenty grains of salt. At dinner, I took six ounces of strong beef soup, eight of roast beef, four of boiled beets, four of bread, two drachms of butter, half a drachm of salt, and drank four ounces of coffee. In addition to this food, I drank daily forty-eight ounces of water, twelve at each meal, and twelve immediately before going to bed.

I thus took daily into my system sixteen ounces of beef, eighteen of bread, six of soup, four of beets, one of butter, one drachm of salt, two of cream, and two of sugar, and drank ten ounces of coffee and forty-eight of water.

The following table contains the results of the experiments instituted under the foregoing conditions. The temperature of the atmosphere during their continuance was in the mean 73.06° Fahrenheit:—

	Weight of body.	Carbonic acid expired.	Aqueous vapor expired.	Feces.	URINE.						
					Quantity.	Free acid.	Urea.	Uric acid.	Chlorine.	Phosphoric acid.	Sulphuric acid.
1st day...	226.41	11760.57	5115.07	8.10	43.42	31.43	664.20	15.37	139.62	55.36	41.56
2d day...	226.40	11973.65	5286.25	8.05	43.05	32.86	658.31	15.41	142.86	55.16	42.53
3d day...	226.35	11428.04	4963.41	8.11	44.10	30.19	666.00	14.29	143.54	56.92	40.60
4th day..	226.44	11467.16	4895.50	8.08	45.03	33.15	673.29	14.03	142.75	54.79	43.26
5th day..	226.43	11745.49	5004.26	8.09	43.69	30.52	682.58	13.81	146.52	53.65	40.35
Average	226.40	11674.98	5052.90	8.08	43.86	31.63	668.87	14.58	144.06	55.17	41.66

The preceding table, therefore, indicates the quantity of carbonic acid, aqueous vapor, feces, urine and its principal constituents excreted, when the weight of the body was nearly uniform, and when no alcohol was taken into the system. During the continuance of these experiments, my general health was excellent. My pulse averaged eighty-one per minute, and was of moderate strength and fullness. My appetite was good, and digestion was performed with regularity.

Having thus ascertained the state of the system as far as my inquiries advanced, when no alcohol was ingested, and when the food was sufficient to sustain the well-being of the organism, I next proceeded to investigate the action of the substance under consideration when all the circumstances which governed the preceding experiments were observed. On the day succeeding their termination, I commenced the second series by taking four drachms of alcohol at each meal, which course was continued for five days. The alcohol was diluted with an equal quantity of water. The other food, and the mental and physical exercise, sleep, etc. remained undisturbed. The mean temperature of the atmosphere was 72.44° .

The annexed table exhibits the results:—

	Weight of body.	Carbonic acid expired.	Aqueous vapor expired.	Feces.	URINE.						
					Quantity.	Free acid.	Urea.	Uric acid.	Chlorine.	Phosphoric acid.	Sulphuric acid.
1st day...	226.64	10527.65	4729.52	7.11	41.90	30.17	591.10	13.21	112.15	33.29	30.87
2d day....	226.95	10474.29	4853.27	6.91	39.71	29.29	585.17	13.18	119.10	35.40	25.84
3d day....	226.80	10256.47	4825.33	6.79	40.24	29.78	562.20	13.98	94.70	28.47	30.19
4th day..	227.06	10175.36	4893.68	6.76	39.88	31.65	586.52	13.24	105.38	30.17	26.24
5th day..	226.81	10289.11	4975.19	6.75	40.45	34.26	583.41	13.12	101.04	26.18	28.18
Average	226.85	10344.57	4855.39	6.86	40.43	31.03	581.68	13.34	106.47	30.70	28.26

Thus, after the use of sixty drachms of alcohol in five days, my weight is seen to have increased from an average of 226.40

pounds to an average of 226·85 pounds, being ·45 of a pound difference. The carbonic acid and vapor of water in the expired air had respectively decreased 1324·50 and 196·51 grains, the feces 1·22 ounces, the urine 3·43 ounces, the urea 87·19 grains, the chlorine 37·59 grains, the phosphoric acid 24·47 grains, and the sulphuric acid 13·40 grains. The free acid and uric acid—especially the former—were so slightly affected as to render it probable that the alcohol had exercised no influence upon them.

The cutaneous transpiration did not appear to be sensibly affected, except upon the third day, when I thought I perceived that it was augmented.

During these experiments, my general health was somewhat disturbed. My pulse was increased to an average of ninety per minute, and was fuller and stronger than previously; there was headache and increased heat of the skin, and my mental faculties were certainly not so clear as on the days when no alcohol was taken. There was also general lassitude, and indisposition to exertion of any kind. My appetite was variable. Digestion was effected as well as previously. The amount of flatus discharged from the intestines was sensibly diminished.

The metamorphosis of tissue and fat was evidently considerably retarded, as is shown in the decreased amount of urea, etc. excreted by the kidneys, and in the lessened quantity of carbonic acid and aqueous vapor given off in respiration. The diminution in the weight of the feces was doubtless mainly owing to the increased assimilation of food induced by the alcohol.

As this substance is incapable of being converted into tissue, the increase in the weight of the body was probably owing to the three following causes:—

1st. The retardation of the decay of the tissues.

2d. The diminution in the consumption of the fat.

3d. The increase in the assimilative powers of the system by which the food was more completely appropriated and applied to the formation of tissue.

From a due consideration of the foregoing experiments, I am disposed to think that, when the food is sufficient for the requirements of the system, alcohol is injurious by exciting the circulation and tending to produce a plethoric habit of body. In these respects its influence is no worse than an excessive amount of food of any kind, or the omission of physical exercise when the system is habituated to its use.

It has been repeatedly shown that muscular exertion accelerates the destruction of the tissues, and Böcker has conclusively proven that the action of water is similar. When, therefore, the aliment ingested is sufficient to maintain the strength and weight of the body, alcohol, if indulged in, should be counteracted in its effects by one or other of the above compensating influences. The action of chloride of sodium is also antagonistic to that of alcohol, and might be similarly employed. By these means the balance of the organism would be preserved.

It is very evident, however, on a careful review of the preceding investigations, that under many circumstances in which man is frequently placed, alcohol might be productive of very beneficial results. The ensuing experiments tend to confirm this observation.

II. The action of alcohol when the body lost weight from deficiency of food.

I ascertained that, by reducing the amount of bread daily taken to twelve ounces, and the meat to ten ounces, the loss of weight in the body was sufficiently well marked. I, therefore, after allowing five days to elapse since the last experiments, instituted another series in which I took two ounces less of each of these substances at each meal. The remaining conditions of food, exercise, etc. continued as in the last series. On the evening previous to commencing these observations my weight was 226·73. The mean temperature of the atmosphere was 73·17°. The following table shows the results of the experiments in detail:—

	Weight of body.	Carbonic acid expired.	Aqueous vapor expired.	Feces.	URINE.						
					Quantity.	Free acid.	Urea.	Uric acid.	Chlorine.	Phosphoric acid.	Sulphuric acid.
1st day...	226.62	11125.54	4759.82	6.02	42.80	28.55	621.50	12.84	126.26	44.30	35.33
2d day....	226.30	10862.29	4681.59	5.98	41.27	27.49	635.22	12.72	135.37	44.10	36.57
3d day....	225.92	10555.70	4600.18	6.05	41.55	30.45	630.43	12.74	130.29	46.08	38.82
4th day..	225.69	10641.65	4610.25	5.96	40.10	26.17	641.34	12.55	120.45	45.51	38.68
5th day..	225.34	10680.90	4687.28	6.00	40.76	26.35	618.18	12.95	129.13	42.24	37.48
Average	225.97	10774.41	4667.82	6.00	41.29	27.80	629.33	12.76	128.00	44.44	37.37

During these experiments my pulse averaged eighty-eight per minute. My general health appeared to be good, except that after exertion I was more exhausted than on the days when full food was taken. My desire for aliment was very much increased, and was never completely appeased by the quantity ingested. The sensible perspiration did not appear to vary from the quantity excreted during the first observations.

I proceeded in the next place to ascertain the effects of alcohol upon my system under circumstances similar to those which existed during the last experiments. With this view I took, on the ensuing day, twelve drachms of alcohol—four drachms at each meal—and continued it for five days. The mean temperature of the atmosphere was 73.34° . The accompanying table exhibits the results:—

	Weight of body.	Carbonic acid expired.	Aqueous vapor expired.	Feces.	URINE.						
					Quantity.	Free acid.	Urea.	Uric acid.	Chlorine.	Phosphoric acid.	Sulphuric acid.
1st day...	225.45	10055.72	4426.18	5.85	40.22	30.10	584.75	14.01	119.17	38.50	33.17
2d day....	225.56	09821.91	4252.75	5.81	39.52	28.56	561.52	13.82	115.24	36.42	34.29
3d day....	225.50	10024.60	4385.90	5.82	39.10	26.14	575.19	14.05	116.91	32.19	31.42
4th day..	225.52	09948.25	4449.68	5.80	40.00	27.19	570.23	14.00	118.14	37.10	29.86
5th day..	225.48	09876.13	4364.36	5.76	40.77	31.24	582.35	14.06	120.43	34.48	27.57
Average	225.50	09945.33	4375.77	5.81	39.92	28.64	574.82	13.99	117.98	35.74	31.26

During the experiments immediately preceding these, my weight decreased an average of $\cdot 28$ of a pound daily, falling from 226.73 pounds to 225.34. In the present series, under the same conditions, except the use of the alcohol, this decrease has not only been overcome, but there is an actual average daily increase of $\cdot 03$ of a pound, the weight rising from 225.34 to a mean of 225.50 pounds. The mean weight of the body is less than the mean of the last series, owing to the fact that the average daily gain is not so great as the previous average daily loss.

The carbonic acid expired is seen to have decreased an average of 729.08 grains, the aqueous vapor 312.06 grains, the feces $\cdot 19$ of an ounce, the quantity of urine 1.37 ounces, the urea 54.51 grains, the chlorine 10.08 grains, the phosphoric acid 8.70 grains, and the sulphuric acid 6.11 grains. The free acid of the urine, and the uric acid, were apparently slightly increased.

The sensible perspiration was not perceptibly affected through the day, but at night it seemed to be somewhat increased. The general condition of my system was never better. My pulse had fallen to an average of eighty-three per minute, there was no headache, the intellectual faculties were clear, and of normal energy, the quantity of food ingested fully satisfied the appetite, sleep was sound and refreshing, and, in fact, all the functions of the organism were performed with regularity. The absence of any symptoms indicating derangement of the health cannot, I think, be ascribed to immunity by continued use of the alcohol, as ten days had elapsed between the two sets of experiments in which it was taken.

The good effects of this substance in limiting the waste of the body, when the supply of food is not sufficient to maintain the vigor of the system, are here very evident, and stand in marked contrast to its influence when an abundance of food was ingested. The strength was not only sustained, but the body gradually

but noticeably gained weight. In short, the alcohol had taken the place of the bread and meat omitted, and at no apparent disadvantage to the general economy. As a compensating agent for a deficiency of food its power cannot, I think, be questioned.

III. The effects of alcohol when the body gained weight from excess of food.

For the purpose of ascertaining the action of alcohol under the above condition of the system, I increased the quantity of meat daily eaten, from sixteen to twenty-two ounces, and the bread, from eighteen to twenty-four ounces. By this addition to the amount of aliment, I found my weight underwent a sensible and tolerably regular increase. The remaining food and mental and physical exertion continued as in the first experiments. Five days were suffered to elapse between this and the last series of investigations. The mean temperature of the atmosphere was 72.06° . The annexed table contains the results of the observations made under the above circumstances:—

	Weight of body.	Carbonic acid expired.	Aqueous vapor expired.	Feces.	URINE.						
					Quan- tity.	Free acid.	Urea.	Uric acid.	Chlo- rine.	Phos- phoric acid.	Sul- phuric acid.
1st day...	225.61	11872.54	4895.32	12.10	43.30	35.63	698.70	17.25	152.18	58.29	50.67
2d day...	225.85	12251.86	5324.48	12.98	45.61	34.71	721.62	16.82	155.21	64.66	50.18
3d day...	226.15	12329.47	5250.79	12.74	45.23	38.23	710.43	17.86	150.59	62.10	51.50
4th day..	226.36	12178.22	5387.20	12.76	46.18	35.45	735.84	18.05	158.25	66.75	48.15
5th day..	226.59	12165.94	5419.68	12.65	45.56	39.28	723.37	18.10	161.03	62.38	49.05
Average	226.11	12159.60	5255.49	12.64	45.17	36.66	718.99	17.61	155.45	62.71	49.91

At ten o'clock on the night before the commencement of the above experiments my weight was 225.50; a slight diarrhœa, which occurred in the interval, had probably rendered it somewhat less than it would otherwise have been. On the last day of the series it was 226.59, showing an increase of 1.09 pounds, which, as all the excreted substances had increased in quantity over the amounts of the first series, could have arisen from no

other cause than the excess of food. The sensible perspiration was also apparently augmented both by day and night.

Symptoms of derangement of the health were more or less present during the continuance of the observations. The pulse was increased in fullness and frequency, averaging ninety-two per minute. There was almost constant headache, indisposition to exertion, and increased desire for sleep, which was, however, frequently disturbed by unpleasant dreams. My appetite was not very good, and after eating there was occasional pain. There was an increased discharge of flatus from the intestines.

On the day succeeding the termination of these investigations, I commenced the following by taking, under the conditions of food, etc. of the last experiments, the fixed quantity of four drachms of alcohol at each meal, which, as previously, was continued for five days. The ensuing table exhibits the results. The mean temperature of the atmosphere was 73·60°.

	Weight of body.	Carbonic acid expired.	Aqueous vapor expired.	Feces.	URINE.						
					Quantity.	Free acid.	Urea.	Uric acid.	Chlorine.	Phosphoric acid.	Sulphuric acid.
1st day...	226·82	12015·37	5384·47	10·40	40·91	38·11	627·58	18·20	128·35	49·82	38·17
2d day...	227·17	11523·19	5090·26	10·22	40·50	36·34	639·60	18·31	121·42	51·27	39·72
3d day...	227·48	11452·71	4829·64	10·38	41·37	34·13	629·41	18·11	126·15	46·14	40·55
4th day..	227·80	11514·23	4831·70	10·18	40·62	39·24	610·17	18·01	135·10	46·98	40·52
5th day..	228·15	11382·50	4810·35	10·35	41·73	35·46	621·86	18·15	131·68	47·51	36·23
Average	227·48	11577·61	4989·28	10·30	41·02	36·65	625·72	18·15	128·54	48·34	39·04

During the series of experiments immediately preceding the present, the average daily increase of weight was ·22 of a pound. By the above table, it is seen that, by the action of the amount of alcohol ingested, the average increase was raised to ·31 of a pound per day. The average amount of carbonic acid excreted, compared with the mean of the last series, was reduced 581·99 grains, the aqueous vapor 266·21 grains, the feces 2·34 ounces, the urine 4·15 ounces, the urea 93·27 grains, the chlorine 26·92

grains, the phosphoric acid 8.29 grains, and the sulphuric acid 14.87 grains. The free acid and uric acid were but slightly affected. The perspiration was sensibly diminished.

While these experiments were progressing, the healthy action of my system was very much disordered. Headache was constant, sleep was disturbed, the skin was hot, pulse full and bounding, averaging ninety-eight per minute, and there was on two occasions, after eating, slight palpitation of the heart. My appetite was capricious. Sometimes disgust was created by the mere sight of food, at other times I ate with a good deal of relish. I think I should have been made seriously ill if I had continued the investigations longer. Upon a return, however, to my ordinary food, all unpleasant symptoms gradually disappeared. This fortunate termination was probably promoted by a diarrhoea of considerable violence, which commenced on the second day after the conclusion of the experiments, and continued forty-eight hours.

The inquiries into the actions of alcohol upon the human economy were now terminated. Upon consideration of the foregoing experiments collectively, I arrive at the conclusion *that alcohol increases the weight of the body by retarding the metamorphosis of the old tissues, promoting the formation of new, and limiting the consumption of the fat.* Viewed in detail, it is seen that, under the use of alcohol, the following effects constantly ensued:—

1st. The carbonic acid and aqueous vapor given off in respiration were lessened in quantity.

2d. The amount of feces was diminished.

3d. The quantity of urine was reduced.

4th. The urea, chlorine, and phosphoric and sulphuric acids were diminished in amount.

These effects, occurring when the amount of food was below the quantity required to maintain the weight of the body under

the mental and physical exercise taken, were productive of no deleterious results to the system. On the contrary, when the food was sufficient to balance the waste from the excretions, and still more so when an excess of aliment over the demands of the organism was ingested, the healthy working of the system was disturbed, and actual disease almost induced.

The use of alcohol, even in moderation, cannot therefore be either exclusively approved or condemned. The laboring man, who can hardly procure bread and meat enough to preserve the balance between the formation and decay of his tissues, finds here an agent which, within the limits of health, enables him to dispense with a certain quantity of food, and yet keeps up the strength and weight of his body. On the other hand, he who uses alcohol when his food is more than sufficient to supply the waste of tissue, and, at the same time, does not increase the amount of his physical exercise, or drink an additional quantity of water—by which the decay of tissue would be accelerated—retards the metamorphosis while an increased amount of nutriment is being assimilated, and thus adds to the plethoric condition of the system which excessive food so generally induces.

The foregoing experiments confirm those of Böcker, so far as the diminution of the carbonic acid expired and the reduction of the solids and water of the urine are concerned. This physiologist, however, found that under the use of alcohol the feces excreted and the water exhaled from the lungs were unaffected. The present investigations, on the contrary, indicate that both the fecal excretion and the water expired were materially diminished. These discrepancies are probably due to the difference in the quantities of alcohol imbibed, the preceding experiments being performed with a much larger amount of this substance than were Böcker's.

The perspiration not having been measured by direct experiment, I have not laid much stress upon the apparent results

obtained. The temperature of the atmosphere was, however, unusually uniform during the continuance of the observations, and any alteration in the quantity of this excretion was doubtless owing to the influence of the alcohol. Yet the liability to form an erroneous opinion, when judging only from the sensations, leaves the action of alcohol upon the cutaneous transpiration still to be definitely determined.

It has been assumed by several late writers that the primary action of alcohol is the retention in the blood of the products of metamorphosis. I am inclined to think this opinion erroneous, and that alcohol, instead of preventing the elimination of the decayed tissues, acts by preventing, in a great measure, their primary destruction. No one will dispute the point that, if the first of these views is correct, alcohol must be uniformly deleterious, and that it must manifest such unmistakable symptoms as could not possibly lead to a misconstruction of its mode of action. If this had been its influence on my own system, what an immense accumulation of carbonized and nitrogenized substances would have been retained in the blood, and what a different set of symptoms would have been experienced! Besides, these symptoms would have been also present during the experiments conducted with alcohol when an insufficient quantity of food was taken; and yet on these days they were entirely absent, and my system was never in better order. Indeed, it may possibly be a question of doubt in the minds of some whether the unpleasant symptoms which were observed were not due as much to excessive food as to the alcohol.

The most strenuous supporter of the theory that alcohol causes the retention of the decomposed tissues in the blood is Dr. Carpenter, and it is with great diffidence that I find myself constrained to differ with so eminent a physiologist. Dr. Carpenter also, while admitting (*Essay on Alcohol*) that there are occasions when it is of importance that an increased amount of mental or

physical exertion should be made, and that under such circumstances alcohol may be temporarily beneficial, ascribes its influence in producing additional nervous force to the fact that it occasions more rapid metamorphosis of the nervous tissues. The experiments detailed in the present paper invariably show a diminished excretion of the products of nervous decay after the exhibition of alcohol, and consequently such cannot be its action.

I do not wish to be understood as at all contending for the propriety of habitual indulgence in alcohol. My experiments show that there are circumstances in which its use is injurious. I believe, however, that these circumstances can be so modified that alcohol may be moderately indulged in without the production of deleterious effects. Full food, insufficient exercise, and alcohol conjoined, will as certainly produce disease if the action of this latter agent is the retardation of tissue-metamorphosis, as though it prevented the elimination from the blood of substances injurious to the organism. On the one hand, however, the affection would be of a sthenic, and on the other of an asthenic character. While, therefore, fully admitting that the use of alcohol requires prudence and discretion, I am not prepared to concede that it is essentially poisonous, or even that there are not conditions of the system in which its employment is not eminently to be commended.

TOBACCO.—The experiments with this substance, though not so full as those with alcohol, were conducted upon the same general principles. They embraced the consideration of its effects under the following conditions:—

I. When the food was sufficient to maintain the healthy balance of the system.

II. When a deficiency of aliment was ingested.

I had previously instituted some experiments, which, though incomplete, were sufficient to indicate the general action of tobacco

upon the organism. They were confirmatory of the present, so far as they extended, which was principally to the relations of the substance under consideration to the urine and its constituents.

As in the experiments with alcohol, I fixed upon a definite and invariable amount of sleep and mental and physical exertion. This was precisely as has been previously stated in detail. The experiments related to the same determinations, and all the analyses were performed in exactly the same manner, and at the same periods of the day as formerly.

After the expiration of twelve days since the investigations into the action of alcohol, and when my system was again in a perfectly normal condition, I commenced the experiments with tobacco. I am not in the habit of using this substance in any form, but had, previous to my observations, smoked an occasional cigar without any perceptible effect resulting, other than slight nervous excitement. I have never in my life chewed tobacco or used snuff.

1st. The effects of tobacco when a sufficiency of food was taken to keep up the weight and vigor of the body.

I lived exactly as in the corresponding series of experiments with alcohol, except that I found it necessary—from, as I suppose, the greater heat of the atmosphere, and consequently the induction of a larger amount of cutaneous transpiration—to increase the quantity of water from forty-eight ounces daily to fifty-two ounces—thirteen at each meal, and thirteen immediately before going to bed. The observations under this mode of living were continued, as before, for five days. The mean temperature of the atmosphere for the period was 80.12° . The following table exhibits the results:—

	Weight of body.	Carbonic acid expired.	Aqueous vapor expired.	Feces.	URINE.						
					Quantity.	Free acid.	Urea.	Uric acid.	Chlorine.	Phosphoric acid.	Sulphuric acid.
1st day...	225.84	11845.29	4827.50	8.12	40.54	29.43	643.18	13.10	151.62	57.42	39.52
2d day....	225.78	11582.73	4855.91	8.10	41.66	27.82	662.27	12.78	155.16	54.38	36.18
3d day....	225.76	11628.65	4986.70	8.11	42.13	30.51	650.30	12.64	144.25	52.29	35.27
4th day..	225.80	11439.26	4758.37	8.07	42.76	26.17	665.14	12.82	142.51	56.77	35.40
5th day..	225.76	11586.40	4994.85	8.09	41.35	25.39	667.58	12.80	150.52	60.06	38.22
Average	225.79	11616.46	4884.66	8.10	41.69	27.86	657.69	12.83	148.81	56.18	36.92

The heat of the atmosphere during the above experiments was 7.06 degrees greater than during the first set of experiments in the alcohol series. My pulse averaged eighty-five per minute. My health, notwithstanding the extreme heat of the weather, was excellent. My appetite was good, and my food was well digested.

Under the same conditions as the experiments just concluded, I proceeded in the next place to ascertain the direct effects of tobacco. With this object, I smoked one hundred and fifty grains of tobacco—nearly two cigars—after each meal, being four hundred and fifty grains per day. During these experiments, the mean temperature of the atmosphere was 78.11°. The annexed table exhibits the results:—

	Weight of body.	Carbonic acid expired.	Aqueous vapor expired.	Feces.	URINE.						
					Quantity.	Free acid.	Urea.	Uric acid.	Chlorine.	Phosphoric acid.	Sulphuric acid.
1st day...	225.81	11726.58	4658.22	8.10	40.21	30.84	628.41	18.29	135.43	58.60	40.59
2d day....	225.87	11562.97	4473.18	8.11	39.63	32.26	610.93	18.80	118.15	84.10	43.17
3d day....	225.86	11839.65	4485.41	8.09	39.80	35.18	614.11	19.03	127.84	75.33	38.65
4th day..	225.90	11710.80	4627.64	8.06	39.45	31.59	604.50	19.01	117.25	81.52	40.10
5th day..	225.85	11482.51	4681.57	8.10	40.02	34.57	618.68	18.45	130.21	70.49	44.15
Average	225.86	11664.50	5585.20	8.09	39.82	32.89	615.32	18.71	125.77	80.01	41.33

Under the use of tobacco, my weight had increased an average of .07 of a pound, the carbonic acid 88.04 grains, the free

acid of the urine 4·93 grains, the uric acid 5·88 grains, the phosphoric acid 23·83 grains, and the sulphuric acid 4·41 grains. On the contrary, the quantity of aqueous vapor had decreased 299·46 grains, the feces ·01 of an ounce, the urine 1·87 ounces, the urea 42·37 grains, and the chlorine 23·04 grains.

The general effects of the tobacco upon my system were exceedingly well marked. There was great nervous excitement, accompanied by irregular action of the muscles, more particularly of the eyelids, mouth, and upper extremities, which lasted for about two hours after each occasion of using this substance. The mind, however, was clear, and there was no headache. These sensations were succeeded by a pleasant feeling of ease and contentment, which also lasted about two hours. During the first part of the night, there was wakefulness, but this was always followed by a sound sleep, which continued till the hour for rising. The pulse was increased to an average of ninety-two per minute. My appetite was as good as usual. The perspiration was apparently slightly diminished.

After allowing five days to elapse, as in former experiments, in order that the system might have time to regain its natural condition, I commenced the observations under the second head, viz.: *the effects of tobacco upon the organism when an insufficiency of food was taken.* I reduced—as in the corresponding experiments with alcohol—the quantity of bread daily ingested to twelve ounces, and the meat to ten ounces. In all other respects, the conditions of the last experiments remained unaltered. During these investigations the mean temperature of the atmosphere was 80·92°. The results are contained in the following table:—

	Weight of body.	Carbonic acid expired.	Aqueous vapor expired.	Feces.	URINE.						
					Quantity.	Free acid.	Urea.	Uric acid.	Chlorine.	Phosphoric acid.	Sulphuric acid.
1st day..	225.58	10672.86	4537.69	6.02	38.74	22.47	623.50	11.58	128.31	45.78	34.54
2d day....	225.20	10384.61	4483.22	6.06	38.20	24.18	615.11	11.23	131.58	43.29	33.09
3d day....	224.79	10350.92	4394.48	6.04	39.04	25.72	604.25	10.01	125.44	44.64	32.22
4th day..	224.33	10526.45	4456.73	6.03	39.57	26.19	601.19	09.82	130.17	42.18	30.15
5th day..	223.97	10347.81	4375.16	6.05	38.73	24.65	608.46	10.04	132.26	45.25	28.31
Average	224.77	10450.53	4449.45	6.04	38.85	24.64	610.50	10.53	129.55	44.23	31.66

The general effects observed were of a similar character to those noticed during the experiments performed under like conditions in the alcohol series. The extreme heat of the weather, however, rendered the amount of sensible perspiration much larger. The pulse was eighty-six per minute. My appetite was always good; but as I always left the table with a feeling of hunger, I felt myself gradually becoming weaker day by day. On the night previous to the commencement of these experiments, my weight was 225.81. On the last day of the series it was 223.97. I had, therefore, lost 1.84 pounds, or an average daily of nearly .37 of a pound.

Under the condition of the system thus produced, I began, on the day following the conclusion of the experiments just detailed, and under circumstances every way identical, the concluding series relative to the effects of tobacco. I smoked, as previously, one hundred and fifty grains of cigars after each meal. The average temperature of the atmosphere was 74.09°. The special results are exhibited in the following table:—

	We ht of body.	Carbonic acid expired.	Aqueous vapor expired.	Feces.	URINE.						
					Quan- tity.	Free acid.	Urea.	Uric acid.	Chlo- rine.	Phos- phoric acid.	Sul- phuric acid.
1st day...	223·80	10568·37	4382·28	4·50	37·85	26·81	569·70	14·91	118·36	72·86	40·21
2d day....	223·65	10495·13	4417·30	4·48	37·29	25·14	541·28	15·11	111·53	75·71	38·02
3d day....	223·55	10265·80	4293·74	4·49	37·15	28·16	536·12	15·29	115·83	78·60	39·00
4th day..	223·56	10483·69	4150·83	4·53	37·48	28·73	552·10	14·80	112·40	74·22	42·23
5th day..	223·54	10478·36	4203·41	4·62	36·92	29·54	540·61	15·17	114·66	70·91	40·58
Average	223·62	10458·27	4289·51	4·52	37·34	27·67	547·96	15·05	114·55	74·46	40·01

From the above table, it is seen that the loss of weight in the body, induced by the deficient supply of food, was lessened from the first, and entirely overcome on the fourth day—the average daily loss being less than ·09 of a pound, against ·37 of a pound, under the same conditions, except the use of tobacco. The excretion of carbonic acid from the lungs was not, in the average, perceptibly affected. The amount of aqueous vapor exhaled was reduced 159·94 grains, the feces 1·92 ounces, the quantity of urine 1·51 ounces, the urea 62·54 grains, and the chlorine 15 grains. The free acid of the urine was increased 3·03 grains, the uric acid 4·52 grains, the phosphoric acid 30·23 grains, and the sulphuric acid 8·35 grains.

The general effects upon the system were almost identical with those previously described as resulting from the former use of tobacco. There was the same nervous excitement, trembling, and wakefulness, but in a somewhat less degree. The pulse was an average of ninety per minute. The desire for food was not nearly so great as in the last experiments, neither was there so great a degree of debility. The cutaneous transpiration, whether from the diminished temperature of the atmosphere or as an effect of the tobacco used, was very sensibly lessened in quantity.

From these experiments the following conclusions are deducible:—

1st. That tobacco does not materially affect the excretion of carbonic acid through the lungs.

2d. That it lessens the amount of aqueous vapor given off in respiration.

3d. That it diminishes the amount of the feces.

4th. That it lessens the quantity of urine, and the amount of its urea and chlorine.

5th. That it increases the amount of free acid, uric acid, and phosphoric and sulphuric acids, eliminated through the kidneys.

These results differ in several essential points from those obtained with alcohol. The fact that the amount of carbonic acid given off in respiration was not diminished, would indicate that the consumption of the fat of the body is not lessened by the use of tobacco. The metamorphosis of the nitrogenous tissues, judging from the diminution in the quantity of urea and chlorine observed, would appear to be retarded, and yet the amount both of the phosphoric and sulphuric acids excreted, especially the former, was very considerably augmented. As both phosphorus and sulphur enter into the composition of all the proteinaceous tissues, it is difficult to reconcile this apparent inconsistency in the results, unless by assuming—what there is great reason to believe—that the oxydation of the phosphorus and sulphur of the brain and nervous tissue was so great in amount as to cause an increase in the elimination of phosphoric and sulphuric acids, even though the metamorphosis of the other nitrogenous tissues was lessened.

The effect produced by tobacco upon the excretion of the free acid and uric acid of the urine was also different from that caused by alcohol. Though both alcohol and tobacco diminish the quantity of urea, the latter only of these substances would appear to exercise any very material influence upon the amount of uric acid eliminated. If there are any definite and constant relations existing between these two constituents of the urine, they would appear to be further from determination than ever.

Tobacco, when the food is sufficient to preserve the weight of

the body, increases the weight; and when the food is not sufficient, and the body in consequence loses weight, tobacco restrains the loss. Unlike alcohol, this influence is unattended with any unpleasant effects upon the circulatory system, though its action on the brain and nerves is certainly not such as always to be desired. When used in greater moderation than in these experiments, this influence would doubtless be greatly lessened.

I refrain from entering into the discussion of the other physiological points connected with the foregoing experiments. A simple examination of the tables will show that these are many and of great interest, and that it is not only as exhibiting the actions of alcohol and tobacco upon the system that the investigations detailed in this paper are valuable; neither have I the time to discuss further the immediate subjects of inquiry.

To that earnest band of physiologists who are constantly investigating the operations of nature, and who rely more upon actual observations than upon abstract theories, I submit these experiments. Though the deductions I have drawn from them may not stand before the progress of physiological research, the materials collected will, I am confident, never entirely lose their value.

NOTE.—The foregoing experiments have been constantly verified by further observations during the last five or six years. I have no hesitation in expressing my opinion that in the great majority of cases the moderate use of alcohol and tobacco is calculated to exert a beneficial effect upon the organism—not the least important influence of tobacco is derived from its action on the salivary glands. It is a well-known fact that whatever increases the amount of saliva secreted increases likewise the quantity of gastric juice. A small quantity of vinegar or tobacco placed in the mouth of a dog with a gastric fistula, invariably causes a flow of gastric juice through the tube in the fistula. Hence the benefit of an after-dinner cigar is not only exerted on the mind, but through the nerves on the secretory apparatus of the stomach.

EXPERIMENTAL RESEARCHES

RELATIVE TO THE NUTRITIVE VALUE AND PHYSIOLOGICAL EFFECTS OF

ALBUMEN, STARCH, AND GUM,

WHEN SINGLY AND EXCLUSIVELY USED AS FOOD.

INTRODUCTION.

FROM the first moment of existence to its termination, two processes are constantly progressing in the healthy organic being. The first of these, Nutrition, is that by which the several tissues of the body are primarily formed, and subsequently developed and nourished; the second, Decay, is the direct antagonist of the former, and through it those portions of the organism which have performed the office in the economy for which they were assimilated are decomposed into simpler substances, and, after undergoing continued metamorphosis, are eventually excreted from the system. The continuation of those forces constitutes life; the cessation of either of them, for even a limited period, induces death.

The present memoir embraces the consideration of these actions, as they occur in the human system, under certain fixed conditions of alimentation, and is especially intended to show, by actual experiments, in what manner they are affected by albumen, starch, and gum, when singly and exclusively used as food.

It does not comport with the character of this essay to enter

into an elaborate detail of the ordinary course and phenomena of nutrition, or of the destructive metamorphosis of the animal tissues; neither would this be necessary, for the works of Liebig, Carpenter, and Draper, and the erndite and philosophical treatise of Lehmann, are so readily accessible to the profession as to render such a proeedure a work of supererogation; yet a few words in relation to some of the principal points connected with them may not be altogether out of place, and, with a statement of the scope of the present investigations, and of the methods employed in the necessary analyses, may serve as an introduction to the more immediate subjects of experiment.

The food which is required by man to maintain a proper degree of activity in the several functional actions of the system, and to repair the waste in the tissues induced by them, may be divided into four classes.

1st. The protein-compounds: albumen, fibrin, casein, gluten, etc., whose most important element is nitrogen, and whose office in the organism is particularly of a histogenetic character.

2d. The fats: which serve for the maintenance of the animal heat by undergoing oxidation into carbonic acid and water, enter into the composition of the primary cells of the tissues, and are probably active agents in the solution and metamorphosis of the nitrogenous articles of food.

3d. The carbo-hydrates: starch, sugar, gum, etc., some of which, like the fats, serve to support the heat of the body, and which, within the system, may undergo transformation into them.

4th. Inorganic substances: under which head are included water and certain minerals which enter essentially into the composition of the blood and tissues.

Besides the above, various other substances, such as alcoholic liquors, coffee, tea, spices, etc., are frequently taken into the stomach with the food, strictly so called, which, though not con-

tributing directly to the nutrition of the body, are yet often serviceable in promoting digestion, and restraining the too rapid waste of the animal tissues.

Though albumen (the type of the protein-compounds) contains carbon, hydrogen, and oxygen, in addition to nitrogen, and is therefore, *par excellence*, the tissue-forming material, it has been determined, by experiments upon the inferior animals, that a sufficiency of such food to sustain vitality for any length of time cannot be assimilated by the digestive organs; and that unless fat, starch, or some other of the respiratory aliments, together with a proper amount of inorganic salts, be also ingested, the animal soon perishes with all the symptoms of starvation.

In order, therefore, to keep the vital functions at their maximum healthy standard of action, it is essential that the food should be so adjusted in quantity and quality as to subserve all the purposes of plastic formations, and, at the same time, maintain the calorific process at its due degree of activity.

Though instinct and experience are generally sufficient to make such an arrangement of aliments as is adequate to fulfill the ordinary requirements of the system, yet observation is constantly teaching us that these guides are not of themselves always correct in their indications, and that disease, and even death, are frequently induced from the want of a more enlightened system of dietetics.

An extensive series of observations is necessary before we can arrange such a system; before we can so proportion the different classes of food to the individual as to be able to determine, *a priori*, how much of each should be ingested under certain defined conditions and circumstances. Such investigations should especially embrace the determination of the quantities and qualities of the egesta under definite conditions of food, mental and physical exercise, sleep, etc.; repeated analyses of the blood

should be made, and at the same time note taken of all the physical, physiological, and pathological circumstances capable of influencing the results. In addition to the correct ideas of nutrition, and the other physiological processes which researches of this nature carried on for a long period would give us, we should also be far advanced toward the attainment of that exactness in medical science to which all our efforts should be directed.

The theory at present received, explanatory of the process by which the disintegration and metamorphosis of the animal substance occurs, may be briefly stated as follows:—

No part or organ of the body can exercise its functions without a certain portion of the tissue entering into its composition losing its vitality. Interstitial death is thus coeval and coexistent with life.

The bodily material which has become devitalized re-enters the circulation, and mingles with the general mass of the blood. "No organized substance, no part of any plant or animal, after the extinction of the vital principle, is capable of resisting the chemical action of air and moisture."* The effete tissue meets in the blood-vessels with both oxygen and water, and also with a temperature which experiment has demonstrated to be that at which decomposition most readily takes place. Under the combined influence of these agents, the worn-out material is resolved into less complex substances, and is at length, under new forms, eliminated from the system.

Four great channels serve to rid the organism of the products resulting from the decay of its component parts: the lungs, through which carbonic acid, water, and a small portion of nitrogen escape; the skin, eliminating principally water, with some carbonic acid and salts; the intestines, through which—in addition to the unassimilated residue of the food—decomposed

* Liebig's *Letters on Chemistry*, London ed. p. 211.

bile, gases, etc. are excreted; and the kidneys, giving exit to water, salts, and especially nitrogenous substances.

As previously remarked, in order to exhibit fully the extent of the nutrition and regressive metamorphosis of tissue in a definite time, and under certain conditions, the ingesta and excreta of the same period should be carefully measured, and the nature and quantities of their several constituents exactly determined. In addition, the weight of the body should be accurately taken at stated intervals during the continuance of the investigations, and observations frequently made of the density, moisture, and temperature of the atmosphere.

The ensuing researches, though conducted generally on this plan, are yet far from being perfect, and can only be regarded as affording approximative results. In the present state of our knowledge, the difficulty, if not impossibility, of estimating accurately the total amount of oxygen abstracted from the inspired air and retained in the system, and the loss from the lungs and the skin separately, is a bar to precise investigation. Nevertheless, I am sensible that the experiments detailed in this memoir will prove valuable as contributing to a fuller understanding of the effects upon the human system of the different articles of food used, and as indicating the value of these substances as aliments.

The investigations were all instituted upon myself. During their continuance, no other food than that experimented with was taken into the system. An interval sufficient to restore the organism to its normal condition was suffered to elapse after each series before the following one was commenced. During this interval, I lived upon a full and nutritious diet, and endeavored so to arrange the ingesta as to supply the economy with those substances which it most needed.

My usual manner of living, during each of the succeeding series of experiments, was as follows:—

I rose from bed at $6\frac{1}{2}$ A.M. and retired at $10\frac{1}{2}$ P.M. Eight hours of the twenty-four were accordingly passed in inactivity, the remaining sixteen were apportioned in the following manner: Eight were occupied in conducting the necessary analyses, and in other work of the laboratory; four were given to chemical and physiological studies; and four were taken up with the duties of my profession, physical exercise, recreation, etc. The exercise was quite limited, consisting of walking about one thousand yards per day. Each period of twenty-four hours is reckoned from 7 A.M. to the same hour the ensuing morning.

The following determinations of the egesta were made for each period of twenty-four hours as above defined:—

I. The quantity of urine.

A. Water.

B. Solids.

a. Urca.

b. Uric acid.

c. Chlorine.

d. Sulphuric acid.

e. Phosphoric acid.

f. Residue of solid matter.

II. The quantity of feces.

A. Water.

B. Solids.

a. Ether extract.

b. Alcohol extract.

c. Water extract.

d. Insoluble residue.

III. The amount of cutaneous and pulmonary transpirations, (calculated.)

Besides these observations on the egesta, the weight of the body was ascertained at the close of each period. Observations

were also made of the state of the pulse and the temperature of the body, three times during the day. The latter was always determined in a room the temperature of which was 60° F., by placing a delicate thermometer under the tongue.

The height of the barometer and thermometer—mean of three observations—is also given for each day.

On the first and last day of each series of researches an analysis of the blood was made.

In addition to the above, microscopical and chemical examinations of the saliva, urine, and feces were often made, which are not referred to, unless unusual results were obtained. Thus the reaction of the saliva was always determined, but is not mentioned, unless it differed from the normal condition by being neutral or acid. The reaction of the urine and feces is not stated, unless it was neutral or alkaline—these excretions being usually acid. The urine was also frequently tested for the presence of albumen and sugar, and submitted to microscopical examination. The feces were likewise often examined with the microscope.

In performing the requisite analysis, I made use of the following methods. It will be seen that, wherever it was practicable, the volumetric process was employed. This was done, not only because it yields more accurate results than the method of precipitating and weighing, but also because it is more easy of execution, and requires less time. I have merely indicated the special methods, without going into detailed descriptions of them.*

Urine.—The whole quantity of this excretion for the twenty-four hours was accurately weighed.

* For full accounts of all the analytical processes made use of in these experiments, and for much other information valuable to those engaged in physiologico-chemical investigations, the reader is referred to Von Gorup-Besanez' *Anleitung zur zoochemischen Analyse*, a work which has not yet found its counterpart in the English language.

The water and solids were estimated by evaporating to as perfect dryness as possible, over sulphuric acid, in the vacuum of an air-pump, a weighed portion of the whole quantity of urine passed in twenty-four hours. The loss of weight indicated the amount of water, and the weight of the residue the quantity of solid matter contained in this portion. By simple calculation, these were found for the total amount of urine evacuated during the day. This process is open to the objection that it is impracticable by it to deprive the specimen of urine of all its water. The quantity of this latter remaining, when a good vacuum is kept up, is, however, very small, and, upon the whole, the results obtained are more exact than when evaporation by heat is practiced, as the decomposition of the urine, which always attends this latter process, is entirely avoided.

The *urea* was determined by a titrated solution of the nitrate of mercury, as originally proposed by Liebig.

The *uric acid*, by precipitation with hydrochloric acid from a known quantity of the urine, and subsequent weighing.

The *chlorine*, by Liebig's method with the nitrate of mercury.

The *sulphuric acid*, by a titrated solution of chloride of barium.

The *phosphoric acid*, by Liebig's process with a titrated solution of perchloride of iron.

The *residue of solid matter* was found by deducting the sum of the above constituents from the total amount of solids.

Feces.—The whole quantity of the twenty-four hours was first accurately weighed.

The *water* and *solids* were determined by taking a known weight of the feces (when more than one stool occurred in the twenty-four hours these were previously well mixed) and evaporating it to dryness in a chloride of calcium bath at a temperature of 220° F., till upon repeated trials it ceased to lose weight.

The loss showed the proportion of water, and the weight of the dry residue that of the solids in the portion submitted to examination. The amount of each in the whole quantity of feces was then calculated from these data.

The *ether*, *alcohol*, and *water extracts* were severally determined as follows:—

A weighed quantity of the dry feces, obtained as above described, was, in the first place, exhausted with ether in Von Bibra's apparatus. The residue was then treated with alcohol of .83 specific gravity, till this substance failed to extract anything more. The substance remaining was then submitted to the action of distilled water till it was thoroughly exhausted. The extracts obtained by these means were then evaporated, dried at the temperature proper for each, weighed, and the quantity of each in the whole amount of dry feces calculated. The sum of the whole quantity of these extracts, deducted from the whole amount of dry feces, gave the insoluble residue.

The amount of loss from the skin and lungs, collectively, was found, when the body lost weight, by adding the amount of loss to the sum of the ingesta, and subtracting from the aggregate the sum of the excretions from the kidneys and intestines. When the body gained weight, the amount of gain was subtracted from the sum of the ingesta, and the sum of the known egesta deducted as before. The result, in either case, was the loss from the skin and lungs.

The weight of the body was determined by a balance capable of turning with the hundredth of a pound, when loaded with 250 pounds.

In the analysis of the blood, I made use of Scherer's method, which embraces the determination of the *water*, *solids*, *albumen*, *extractive*, and *salts* of the *serum separately*, and the *water*, *solids*, *fibrin*, *blood corpuscles*, *albumen*, *extractive*, *salts*, and *fat* of the *blood as a whole*. Scherer's process, though not al-

together free from objection, is pronounced by Professor Lehmann* to be the best we at present possess.

The microscope employed in these researches was a very fine one of Powell and Lealand's construction, with object-glasses ranging from 1 to $\frac{1}{8}$ inch focal distance.

It is proper that I should state that I am $28\frac{1}{2}$ years of age, 6 feet 2 inches in height, and measure $33\frac{1}{2}$ inches around the most prominent part of the chest. My weight during the last three years has ranged from 215 to 230 pounds. My habit of body is rather full, temperament sanguineo-nervous. I am of sedentary habits, rarely taking much physical exercise, unless with some specific object in view other than the exercise. I have never indulged freely in alcoholic liquors, and very seldom use them now; tobacco I do not use in any form. For the last three years my health has been excellent. For a year previous to this period, I was troubled with symptoms indicative of disease of the heart, but no organic affection could be discovered on thorough examination, and by care and change of air I entirely recovered. At the time of commencing these experiments my health was never better.

In order to show the usual condition of my system, and of the several excretions, and thus to afford data on which to base a more correct estimate of the effects of the several articles of food experimented with than could otherwise be formed, I instituted upon myself a preliminary series of investigations, the details of which are here stated.

During this prefatory series of researches, I ate such articles of food as my appetite called for. It was, as I found by experience, almost impossible to measure the quantities of the different alimentary substances ingested, when, as in this instance, no fixed rule of diet was adopted. The liquids, however, were susceptible

* Physiological Chemistry, vol. i. p. 593, Am. ed.

of easy approximate determination, and the quantities of these are accordingly stated.

The apportionment of the day, as regarded mental and physical exercise, recreation, sleep, etc., was the same as previously stated, and the conditions generally as arranged for the main subjects of inquiry were not materially altered.

In this, and in each of the succeeding series of experiments, all figures expressive of the quantities of the ingesta, egesta, and constituents of the latter refer to Troy grains. The weight of the body is given in pounds and hundredths avoirdupois.*

This series continued five days. As the total weight of the daily ingesta was not determined, no measurement of the loss from the skin and lungs could be made in these investigations.

FIRST DAY.

INGESTA.

Breakfast—Hot bread and butter, and beef-steaks.

Luncheon—Cold beef, and bread and butter.

Dinner—Beef soup, roast beef, potatoes, macaroni, and custard.

During the day drank 4420 grains coffee, and 17250 water.

EGESTA.

Kidneys.

Whole quantity of urine 20258·68.

Water.....	19185·48
Solids.....	1073·20
Urea.....	628·85
Uric acid.....	13·27
Chlorine.....	124·50
Sulphuric acid.....	45·86
Phosphoric acid.....	60·13
Residue.....	210·59

Intestines.

Whole quantity of feces 2310·47.

Water.....	1702·37
Solids.....	608·10

* The pound Avoirdupois is equivalent to 7000 grains Troy. The hundredth is consequently 70 grains Troy.

Ether extract.....	75.94
Alcohol extract	111.38
Water extract.....	128.32
Insoluble residue.....	292.36

My pulse was at 7 A.M. 85 per minute, at 2 P.M. 88, and at 10 P.M. 80.—Mean 84.33.

The temperature of the body at the same hours was respectively 97.5°, 98°, and 98°.—Mean 97.83°.

At 3 P.M. 1525.73 grains of blood were drawn from the median basilic vein. This, upon analysis, was found to be constituted as follows:—

1000 parts of serum—	1000 parts of blood—
Water..... 908.42	Water..... 780.29
Solids..... 91.58	Solids..... 219.71
Albumen..... 76.18	Fibrin..... 2.41
Extractive..... 4.27	" Blood corpuscles... 143.19
Soluble salts..... 10.22	Albumen..... 65.43
	Extractive..... 4.02
	Soluble salts..... 9.11
	224.16
Difference..... .91	Difference..... 4.35
In 1000 parts of serum were contained 11.92 of inorganic salts.	The whole quantity of inorganic salts in 1000 parts of blood was 11.68. In 1000 parts defibrinated blood were 2.24 fat.

The weight of the body at the end of the twenty-four hours was 226.45 pounds. The mean height of the barometer was 29.211 inches, and of the thermometer 43°.

SECOND DAY.

INGESTA.

Breakfast—Buckwheat cakes and butter, broiled ham, boiled eggs.

Luncheon—Cold ham, and bread and butter.

Dinner—Beef soup, roast beef, potatoes and beets.

Drank 5900 grains of coffee, and 18200 water.

EGESTA.

Kidneys.

Whole quantity of urine 22756·37.

Water.....	21488·15
Solids.....	1286·22
Urea.....	790·11
Uric acid.....	10·58
Chlorine.....	151·28
Sulphuric acid.....	50·72
Phosphoric acid.....	66·13
Residue.....	199·40

Intestines.

Whole quantity of feces 2445·69.

Water.....	1681·68
Solids.....	764·01
Ether extract.....	142·40
Alcohol extract.....	125·18
Water extract.....	202·41
Insoluble residue.....	294·02

At 7 A.M. my pulse was 82, at 2 P.M. 90, and at 10 P.M. 83.—Mean 85.

At the same periods, the temperature of the body was respectively 98°, 98·5°, and 98·5°.—Mean 98·33°.

At the end of the twenty-four hours my weight was 226·52 pounds; showing an increase of ·07 pound, or 490 grains.

The mean height of the barometer was 29·341 inches, of the thermometer 46°.

The quantity of food ingested on this day was somewhat greater than usual. Toward evening I had slight headache, which, however, disappeared before bedtime; slept well.

THIRD DAY.

INGESTA.

Breakfast—Hot bread and butter, and beef-steak.*Luncheon*—Cold ham, and bread and butter.*Dinner*—Beef soup, roast chicken, potatoes and cabbage, rice pudding, with wine sauce.

Drank in the twenty-four hours 4250 grains of coffee, and 23500 water.

EGESTA.

Kidneys.

Whole quantity of urine 21250·17.

Water.....	20224·47
Solids.....	1025·70
Urea.....	620·50
Uric acid.....	11·57
Chlorine	142·19
Sulphuric acid.....	35·71
Phosphoric acid.....	47·31
Residue.....	168·42

Intestines.

Whole quantity of feces 2041·76.

Water.....	1537·63
Solids.....	504·13
Ether extract.....	89·14
Alcohol extract	95·17
Water extract	112·35
Insoluble residue.....	207·47

The pulse at 7 A.M. was 81, at 2 P.M. 86, and at 10 P.M. 84.—
Mean 83·66.

The temperature of the body at the corresponding hours was
respectively 98°, 98·5°, and 97·5°.—Mean 98°.

At the end of the day the weight of the body was 226·42
pounds; a loss from the previous day of ·10 pound, equivalent
to 700 grains.

The mean height of the barometer was 29·241 inches, and of
the thermometer 41°.

FOURTH DAY.

INGESTA.

Breakfast—Hot bread and butter, and beef hash, highly seasoned.*Luncheon*—Cold beef tongue, and bread and butter.*Dinner*—Stewed beef, potatoes, macaroni, and blanc-mange.

Ate also a *supper* at 10 P.M. of oysters (preserved in hermetically sealed
cans) and bread and butter.

Drank in the twenty-four hours 5000 grains of coffee, and 21500 water.

EGESTA.

Kidneys.

Whole quantity of urine 20523·45.

Water.....	19388·27
Solids.....	1134·18
Urea.....	710·62
Uric acid.....	10·91
Chlorine	131·46
Sulphuric acid.....	44·32
Phosphoric acid.....	53·87
Residue.....	183·00

Intestines.

Whole quantity of feces 2204·11.

Water.....	1472·89
Solids.....	731·22
Ether extract.....	60·39
Alcohol extract	67·48
Water extract.....	106·17
Insoluble residue.....	497·18

At 7 A.M. my pulse was 81, at 2 P.M. 84, and at 10 P.M. 82.—
Mean 82·33.

At the same hours the temperature of the body was respectively 97°, 97·5°, and 98°.—Mean 97·50°.

The weight of the body at the end of the twenty-four hours was 226·50 pounds; an increase of ·08 pound, equivalent to 560 grains.

The height of the barometer was 28·965 inches, and of the thermometer 40°.

FIFTH DAY.

INGESTA.

Breakfast—Hot buckwheat cakes and butter, and beef-steak.

Luncheon—Cold ham, and bread and butter.

Dinner—Beef soup, roast venison, potatoes, cabbage, and macaroni, pre-served citron-melon, and milk.

During the day drank 4800 grains of coffee, and 20200 water.

EGESTA.

Kidneys.

Whole quantity of urine 19684.92.

Water.....	18698.29
Solids.....	986.63
Urea.....	521.75
Uric acid.....	12.02
Chlorine.....	141.26
Sulphuric acid.....	49.30
Phosphoric acid.....	51.84
Residue.....	210.46

Intestines.

Whole quantity of feces 2467.58.

Water.....	1975.41
Solids.....	492.17
Ether extract.....	85.14
Alcohol extract	83.60
Water extract.....	98.52
Insoluble residue.....	224.91

My pulse at 7 A.M. was 83, at 2 P.M. 88, and at 10 P.M. 85.—
Mean 85.33.

The temperature of the body at the same periods was respectively 98°, 98.5°, and 97.5°.—Mean 98°.

At 3 P.M. I abstracted 1293.25 grains of blood from the median basilic vein, which, upon analysis, was found to possess the following constitution:—

1000 parts of serum—

Water.....	909.57
Solids.....	90.43
Albumen	72.21
Extractive.....	5.32
Soluble salts.....	12.14
	89.67
Difference... ..	.76

The total amount of inorganic salts
in 1000 parts of serum was 14.39.

1000 parts of blood—

Water.....	782.46
Solids.....	217.54
Fibrin.....	2.36
Blood corpuscles...	141.25
Albumen.....	62.10
Extractive	4.25
Soluble salts.....	11.40
	221.36
Difference.....	3.82

The total amount of inorganic salts
in 1000 parts of blood was 13.75.
In 1000 parts of defibrinated blood
were 2.78 of fat.

The weight of the body at the close of the twenty-four hours was 226·41 pounds; a loss of ·09 pound, or 630 grains.

The mean height of the barometer was 29·042 inches, and of the thermometer 45°.

The following table exhibits the foregoing results in a collected form.

TABLE I.

EGESTA.	1st day.	2d day.	3d day.	4th day.	5th day.	Total.	Mean.
<i>Kidneys—</i>							
Urine.....	20258·68	22756·37	21250·17	20523·45	19684·92	104493·59	20898·71
Water.....	19185·48	21485·15	20224·47	19388·27	18698·29	99005·66	19801·13
Solids.....	1073·20	1268·22	1025·17	1134·18	986·63	5487·93	1097·58
Urea.....	628·85	790·11	620·50	710·62	521·75	3471·83	694·36
Uric acid.....	13·27	10·55	11·57	10·91	12·02	58·35	11·07
Chlorine.....	124·50	151·28	142·19	131·46	141·26	690·69	138·13
Sulphuric acid.....	45·86	50·72	35·71	44·32	49·30	225·91	45·18
Phosphoric acid.....	60·13	66·13	47·31	53·87	51·84	229·28	55·85
Residue.....	210·59	199·40	168·42	183·00	210·46	971·87	194·37
<i>Intestines.</i>							
Feces.....	2310·47	2445·69	2041·76	2204·11	2467·58	11469·61	2293·92
Water.....	1702·37	1681·68	1537·63	1472·89	1975·41	8369·98	1673·99
Solids.....	608·10	764·01	504·13	731·22	492·17	3099·63	619·92
Ether extract.....	75·94	142·40	89·14	60·39	85·14	453·01	90·60
Alcohol extract.....	111·38	125·18	95·17	67·48	83·60	482·81	95·56
Water extract.....	128·32	202·41	112·35	106·17	98·52	647·77	129·55
Insoluble residue.....	292·36	294·02	207·47	497·18	224·91	1575·94	303·18
Weight of body.....	226·45	226·52	226·42	226·50	226·41	226·46
Pulse.....	84·33	85·00	83·66	82·83	85·33	84·23
Temperature of body.....	97° 83'	98° 33'	98°	97° 50'	97° 50'	97° 83'
Barometer.....
Thermometer.....

I now proceed to consider the main subjects of investigation, regretting, however, that they are not treated in a more complete manner, but indulging the hope that the time and labor I have bestowed upon them may not prove altogether without profit to physiological science, and that others, more learned and with greater facilities at their command, will labor to dispel the darkness which yet obscures so many of the vital processes.

I.

ALBUMEN.

It is an established fact in physiology, that nitrogen is essential to the formation of all the organized tissues of the body. The experiments of Regnault and Reiset* have definitely determined, what had previously been arrived at by Boussingault† in another way, that this substance is not absorbed into the system from the atmosphere by respiration, but that there is actually, on the contrary, a loss of nitrogen to the organism from the lungs. It must, therefore, be entirely derived from the alimentary substances ingested into the stomach.

It results, therefore, that food, to be fully available for the requirements of life, must contain nitrogen in its composition, and it was, until recently, contended by many physiologists that the nutritive value of aliments was to be directly measured by the proportion of this element entering into their constitution. It is now, however, generally admitted that in order to conduce to the nutrition of the tissues, the nitrogen must be introduced in the form of protein.

The proteinaceous compounds ordinarily met with in the food of man are albumen, fibrin, casein, vitellin, gluten, and legumin. The first four of these are found in animal, the latter two in vegetable food. Both the organic kingdoms of nature thus unite in providing substances containing protein, and, accordingly,

* *Recherches chimiques sur la respiration.* Paris, 1849.

† *Mémoires de chimie agricole et de physiologie.* Paris, 1854, pp. 1-47.
First published in *Ann. de Chim. et de Phys.*

whether we consider the purely carnivorous or herbivorous animal, we find that each is furnished with aliment containing a sufficiency of nitrogen to serve all the purposes of its organism.

Though the protein aliments are of such great value as organo-plastic materials, it would appear, judging from experiments upon the inferior animals, that life cannot be sustained for any considerable period upon either of them alone. Tiedemann and Gmelin found it impossible to support life in geese which they fed upon pure white of egg, and the researches of other physiologists have yielded similar results. The main difficulty appears to have been the inability of the digestive organs of the animals submitted to experiment, to assimilate a sufficient quantity of a protein compound to afford enough carbon to compensate for the loss of this substance from the lungs. Thus Boussingault* fed ducks exclusively upon albumen, casein, and fibrin, and invariably found this to be the case. Too much importance, however, should not be attached to experiments of this nature. Various temporary causes affecting the solubility of the food may have existed, and great care should be exercised before deducing inferences, and applying them to man, from investigations instituted on the lower animals. The theory—based as it is solely on experiments upon animals far lower in the scale of creation than man—that the digestive fluids can only dissolve a limited amount of an albuminate in a given time, and that this quantity is insufficient for the demands of the system, is far from established, and has been in a great measure disproved by the recent observations of Jones.†

Though differing in physical characteristics, the proteinaceous substances are probably identical in chemical constitution. Albu-

* Op. cit. p. 233, et seq

† Digestion of Albumen and Flesh, etc.—Medical Examiner, 1856, p. 257.

men, the most important of them, may be regarded as the representative of the class. It is one of the chief organic constituents of the chyle and blood, from which all the tissues are elaborated, and no doubt exists that, by some means or other, the remaining members of the group, when taken into the stomach, undergo conversion into it. I have, therefore, selected it for experiment in preference to either of the others.

The investigations into the value of albumen as an article of food, and its effects upon the system, continued ten days. During this period no other solid food was taken into the stomach, and no liquid but water. The albumen used was obtained from the serum of bullock's blood, by boiling it, and was consequently ingested in the coagulated form. This was the only source at my command for obtaining albumen in any quantity. It was well washed, to remove, as far as possible, all extraneous matters, and was then subjected to a temperature of 220° F., in a chloride of calcium bath, to expel all moisture. The water drunk was either distilled or obtained by melting snow. The water of this region,* from the springs and streams, contains so large a proportion of salts that, had it been used, it would have interfered materially with the results. The distilled water was always well agitated with atmospheric air before being drunk. The other conditions under which the investigations were conducted have been fully stated in the Introduction, and need not, therefore, be dwelt upon here. I omitted, however, to state that the feces were usually evacuated immediately after rising in the morning. All deviations from this rule are specially mentioned.

At the termination of the twenty-four hours, immediately preceding the commencement of the experiments, my weight was 226.51 pounds.

* Fort Riley, Kansas.

FIRST DAY.

INGESTA.

8 A.M.	Albumen.....	2980	Water.....	7528
1 P.M.	“	2562	“	6350
5 P.M.	“	3187	“	9580
Total	“	8729	“	23458

EGESTA.

Kidneys.

Whole quantity of urine 16520·36

Water.....	15363·07
Solids.....	1157·29
Urea.....	812·16
Uric acid.....	21·39
Chlorine	30·54
Sulphuric acid.....	28·65
Phosphoric acid.....	36·17
Residue.....	238·38

Intestines.

Whole quantity of feces 1251·70.

Water.....	943·41
Solids.....	308·29
Ether extract	26·25
Alcohol extract	89·74
Water extract.....	125·18
Insoluble residue.....	67·23

Skin and Lungs.

Total loss through these channels 15059·14.

The pulse at 7 A.M. was 82, at 2 P.M. 84, and at 10 P.M. 86.—
Mean 84.

The temperature of the body at the corresponding hours was
respectively 96·5°, 97°, and 98·5°.—Mean 97·33°.

At 3 P.M. I abstracted 1525·80 grains of blood from the median
basilic vein, which, upon analysis, was found to possess the fol-
lowing composition:—

1000 parts of serum—

Water	906.28
Solids	93.72

Albumen.....	78.21
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Extractive.....	6.03
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Soluble salts.....	8.34
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	92.68
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Difference.....	1.04
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The whole quantity of inorganic salts in 1000 parts of serum was 10.29.

1000 parts of blood—

Water	776.45
Solids	223.55

Fibrin.....	2.65
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Blood corpuscles...	142.09
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Albumen	67.00
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Extractive.....	5.11
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Insoluble salts	6.37
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	223.22
--	--------

Difference33
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The whole quantity of inorganic salts in 1000 parts of blood was 7.93.

In 1000 parts of defibrinated blood were 2.33 of fat.

The weight of the body at the close of the twenty-four hours was 226.20 pounds; a loss, therefore, of .31 pound, equivalent to 2170 grains, of which 1525.80 are accounted for by the blood drawn for analysis, leaving 644.20 grains as the actual loss from the excretions.

The mean height of the barometer was 29.277 inches, and of the thermometer 45° F.

My appetite on this day was as good as usual. The food was sufficient to satisfy it, and was by no means unpleasant to the taste. I had no disagreeable symptoms of any kind. Sleep was sound and refreshing, and the intellectual faculties clear.

SECOND DAY.

INGESTA.

8 A.M.	Albumen.....	3250
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1 P.M.	“	2428
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5 P.M.	“	2975
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Total	“	8653
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Water.....	8050
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“	7525
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“	9200
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“	24775
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EGESTA.

Kidneys.

Whole quantity of urine 16937.62.

Water.....	15687.44
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Solids.....	1250.18
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Urea.....	922.89
Uric acid.....	22.47
Chlorine.....	21.54
Sulphuric acid.....	23.65
Phosphoric acid.....	34.17
Residue.....	225.96

Intestines.

Whole quantity of feces 1858.69.

Water.....	1070.94
Solids.....	282.75
Ether extract.....	18.20
Alcohol extract.....	75.32
Water extract.....	124.10
Insoluble residue.....	71.13

Skin and Lungs.

Total loss through these channels 15556.69.

The pulse at 7 A.M. was 84, at 2 P.M. 87, and at 10 P.M. 88.—
Mean 86.33.

The temperature of the body at the same hours was respectively 98°, 98.5°, and 97.5°.—Mean 98°.

My weight at the end of the twenty-four hours was 226.14 pounds; being a loss from the previous day of .06 pound, or 420 grains.

The mean heights of the barometer and thermometer were respectively 29.098 inches, and 42.50°.

I had no unusual feelings of any kind on this day; slept well.

The feces were of a very dark-brown color, and of neutral reaction. Crystals of ammonio-magnesian phosphate, epithelial cells, and oil and mucus globules visible with the microscope.

THIRD DAY.

INGESTA.

8 A.M.	Albumen.....	3760	Water.....	8325
1 P.M.	“	3000	“	8490
5 P.M.	“	4525	“	8420
Total	“	11285	“	25235

EGESTA.

Kidneys.

Whole quantity of urine 18428·60.

Water.....	17039·02
Solids.....	1389·68
Urea.....	1162·39
Uric acid.....	28·92
Chlorine.....	10·45
Sulphuric acid.....	29·18
Phosphoric acid.....	48·21
Residue.....	110·42

Intestines.

Whole quantity of feces 1628·17.

Water.....	1273·91
Solids.....	354·26
Ether extract.....	12·40
Alcohol extract.....	69·27
Water extract.....	99·68
Insoluble residue.....	172·91

Skin and Lungs.

Total loss from these channels 15903·23.

My pulse was at 7 A.M. 86, at 2 P.M. 88, and at 10 P.M. 89.—
Mean 87·66.

The temperature of the body at the same periods was respectively 98°, 97·5°, and 98·5°.—Mean 98°.

At the termination of the twenty-four hours my weight was 226·22 pounds; a gain over the previous day of ·08 pound, or 560 grains.

The mean height of the barometer was 29·245 inches, and of the thermometer 44°.

Two evacuations of the intestinal canal occurred on this day: one at 9 P.M., the other at the regular hour. Both were in appearance, reaction, etc. similar to the discharge of the preceding day. In the evening I had slight pains in the lower part of the abdomen, and quite severe headache. Both disappeared after the first passage from the bowels. My sleep was unquiet in the early part of the night, and I awoke in the morning with headache.

In increasing so materially the quantity of albumen ingested on this day, my main object was to test more completely the power of the digestive organs. It is seen that they were fully capable of dissolving it, and that through its assimilation, enough carbon was absorbed to supply the wants of the system. This is evidenced by the increase in the weight of the body and the augmentation in the quantity of matter eliminated through the skin and lungs.

FOURTH DAY.

INGESTA.

8 A.M.	Albumen.....	4200	Water.....	8560
1 P.M.	“	4650	“	9255
5 P.M.	“	3875	“	6350
Total	“	12725	“	24165

EGESTA.

Kidneys.

Whole quantity of urine 17483·75.

Water.....	15954·25
Solids.....	1429·50
Urea.....	1251·32
Uric acid.....	27·40
Chlorine.....	5·37
Sulphuric acid.....	21·18
Phosphoric acid.....	22·29
Residue.....	101·94

Intestines.

Whole quantity of feces 1827·16.

Water.....	1389·73
Solids.....	437·43
Ether extract	10·36
Alcohol extract	80·29
Water extract.....	151·47
Insoluble residue.....	195·31

Skin and Lungs.

Total loss through these channels 16329·09.

At 7 A.M my pulse was 86, at 2 P.M. 90, and at 10 P.M. 98.—
Mean 91·33.

At the same hours the temperature of the body was respectively 98° , 99° , and 99.5° .—Mean 98.83 .

At the end of the twenty-four hours my weight was 226.32 pounds; an increase of 0.10 pound, or 700 grains.

The mean heights of the barometer and thermometer were respectively 29.230 inches, and 47.66° .

I had severe headache the whole of this day, attended with some fever. The skin was hot and dry. My appetite was not good. After each time of ingesting the albumen there was a feeling of debility in the system, accompanied with a singular sinking sensation at the epigastrium. There was also nausea at several periods of the day. The pains in the lower part of the abdomen were very severe, especially about two hours after each meal.

The feces were similar in appearance to those of the previous day; the reaction was alkaline. Crystals of ammonio-magnesian phosphate in small quantity visible with the microscope.

The urine was of high color, and of strong acid reaction—a drop evaporated to dryness on a slip of glass and placed upon the stage of the microscope, exhibited numerous needle-shaped crystals of urea.

It is perceived from the record of these experiments, that the digestive organs were capable of dissolving the large amount of albumen ingested, and that it was fully sufficient for the support of the respiratory process, and to maintain the weight of the body. The constitutional disturbance induced, warned me, however, against a repetition of so large a quantity.

FIFTH DAY.

INGESTA.

8 A.M.	Albumen.....	1850	Water.....	8250
1 P.M.	“	2330	“	7380
5 P.M.	“	2500	“	8650
Total	“	6680	“	24550

EGESTA.

Kidneys.

Whole quantity of urine 18738.50.

Water.....	17699.08
Solids.....	1039.42
Urea.....	721.26
Uric acid.....	18.40
Chlorine.....	5.01
Sulphuric acid.....	15.12
Phosphoric acid.....	17.25
Residue.....	262.38

Intestines.

Whole quantity of feces 1726.54.

Water.....	1379.30
Solids.....	347.24
Ether extract.....	17.29
Alcohol extract.....	167.52
Water extract.....	85.68
Insoluble residue.....	76.75

Skin and Lungs.

Total loss from these channels 13394.96.

At 7 A.M my pulse was 90, at 2 P.M. 93, at 10 P.M. 104.—
Mean 95.66.

At the same periods the temperature of the body was respectively 97° , 97° and 97.5° .—Mean 97.16° .

At the end of the twenty-four hours my weight was 225.93 pounds; being a loss from the preceding day of .39 pound, equivalent to 2730 grains.

The mean height of the barometer was 29.207 inches, and of the thermometer 42.33° .

On this day I felt far from well. I had headache, and pains in the abdomen. The sinking sensation at the epigastrium was not so great as on the previous day.

Three evacuations of the bowels occurred: one at 10 A.M., one at 4 P.M., and one at 11 P.M. They were thinner, and of a darker color than previously. My physical strength was much less than usual. Appetite was not good. The sight of the

albumen created disgust and nausea. Was quite restless in the night, and felt chilly toward morning. The mental faculties were not sensibly affected.

SIXTH DAY.

INGESTA.

8 A.M.	Albumen.....	2500	Water.....	7530
1 P.M.	“	1520	“	8200
5 P.M.	“	2000	“	7550
Total	“	6020	“	23280

EGESTA.

Kidneys.

Whole quantity of urine 17530·24.

Water.....	16551·88
Solids.....	978·36
Urea.....	728·54
Uric acid	29·17
Chlorine	4·22
Sulphuric acid.....	12·18
Phosphoric acid.....	18·45
Residue.....	175·80

Intestines.

Whole quantity of feces 1852·15.

Water.....	1331·34
Solids.....	520·81
Ether extract.....	10·42
Alcohol extract	112·16
Water extract.....	136·58
Insoluble residue.....	261·15

Skin and Lungs.

Total loss through these channels 12927·61.

At 7 A.M. my pulse was 92, at 2 P.M. 93, and at 10 P.M. 93.—Mean 92·66.

At the same hours the temperature of the body was respectively 96·5°, 97°, and 97·5°.—Mean 97°.

At the end of the twenty-four hours my weight was 225·50 pounds; being a loss of ·43 pound, or 3010 grains.

The mean height of the barometer was 29·110 inches, and of the thermometer 42°.

I experienced on this day an increase of debility. The headache and pain in the abdomen of the preceding days were not present on this. I had very great desire for other food. The albumen was not at all relished, and it was with great effort I could bring myself to eat it. At night I slept quite well.

SEVENTH DAY.

INGESTA.

8 A.M.	Albumen.....	3250	Water.....	8000
1 P.M.	“	4000	“	8500
5 P.M.	“	3550	“	7285
Total	“	10800	“	23785

EGESTA.

Kidneys.

Whole quantity of urine 16592·83.

Water.....	15911·08
Solids.....	581·75
Urea.....	390·60
Uric acid.....	11·28
Chlorine	3·61
Sulphuric acid.....	10·73
Phosphoric acid.....	13·17
Residue	152·36

Intestines.

Whole quantity of feces 3276·40.

Water.....	2122·60
Solids.....	1153·80
Ether extract.....	11·92
Alcohol extract	100·65
Water extract.....	75·10
Insoluble residue.....	955·13

Skin and Lungs.

Total loss from these channels 17476·77.

My pulse was at 7 A.M. 93, at 2 P.M. 94, and at 10 P.M. 95.—
Mean 94.

At the same hours the temperature of the body was respectively 97·5°, 97·5°, and 97·°—Mean 97·33°.

At the termination of the twenty-four hours my weight was

225·10 pounds; a loss, therefore, of 40 pound, equivalent to 2800 grains.

The mean height of the barometer was 29·106 inches, and of the thermometer 35·33°.

I felt weaker on this day than on any previous one of the investigations. Otherwise, I experienced no very disagreeable sensations. My skin was moist and cool during the whole day. Mental faculties active and clear.

There were two evacuations from the bowels: one at 7 P.M., the other at the usual hour. Both were of firm consistence, of the same dark-brown color, and free from strong odor. On heating a small quantity of the urine in a test tube—as had been done each day of the investigations—a precipitate, insoluble in nitric acid, ensued. This was therefore albumen.

EIGHTH DAY.

INGESTA.

8 A.M.	Albumen.....	2980	Water.....	7900
1 P.M.	“	1855	“	8280
5 P.M.	“	3730	“	9525
Total	“	7575	“	25705

EGESTA.

Kidneys.

Whole quantity of urine 21235·18.

Water.....	20407·96
Solids.....	827·22
Urea.....	492·20
Uric acid.....	18·49
Chlorine	3·35
Sulphuric acid.....	11·24
Phosphoric acid.....	11 08
Residue.....	290·86

Intestines.

Whole quantity of feces 3684·02.

Water.....	2373·10
Solids.....	1310·92

Ether extract.....	8.01
Alcohol extract.....	105.27
Water extract.....	122.53
Insoluble residue.....	1075.11

Skin and Lungs.

Total loss from these channels 12770.80.

At 7 A.M. my pulse was 92, at 2 P.M. 91, and at 10 P.M. 89.—
Mean 90.66.

The temperature of the body at the same hours was respectively 97°, 96.5°, and 96°.—Mean 96.50°.

My weight at the end of the twenty-four hours was 224.47 pounds; being a decrease of .63 pound, equivalent to 4410 grains.

The mean heights of the barometer and thermometer were respectively 29.289 inches, and 35.33°.

With the exception of the debility, I felt tolerably well on this day. I did not, however, read or study any, and took no physical exercise beyond walking a few steps.

Two evacuations of the bowels occurred: one at 6 P.M., and the other at the usual hour. The feces were quite hard and similar in color and odor to those of the preceding days.

Albumen was precipitated from the urine by heat. The quantity was considerable.

NINTH DAY.

INGESTA.

8 A.M.	Albumen.....	2150	Water.....	5250
1 P.M.	“	2200	“	5690
5 P.M.	“	1800	“	6000
Total	“	6150	“	16940

EGESTA.

Kidneys.

Whole quantity of urine 12325.10.

Water.....	11674.86
Solids.....	650.24
Urea.....	329.75
Uric acid.....	14.81
Chlorine	2.39

Sulphuric acid.....	8.96
Phosphoric acid.....	10.53
Residue.....	283.80

Intestines.

Whole quantity of feces 8726.50.

Water.....	8106.35
Solids.....	620.15
Ether extract.....	11.24
Alcohol extract.....	162.95
Water extract.....	50.17
Insoluble residue.....	395.79

Skin and Lungs.

Total loss from these sources 10018.40.

My pulse at 7 A.M. was 96, at 2 P.M. 98, and at 10 P.M. 104.—
Mean 99.33.

At the same hours, the temperature of the body was respectively 96°, 96.5°, and 97°.—Mean 96.50°.

The weight of the body at the close of the twenty-four hours was 223.33 pounds; a loss of 1.14 pound, or 7980 grains.

The mean height of the barometer for the day was 29.235 inches, and of the thermometer 24.33°.

A serous diarrhœa of considerable violence commenced on this day. I had six evacuations of the intestines. The discharges were very thin, of a dark-brown color, and faint odor. The debility was much increased. There was dryness of the skin, and the urine was of high color. An increased amount of albumen was present in this latter excretion. My appetite was not good, neither was there much thirst. Mind clear, sleep very unquiet.

TENTH DAY.

INGESTA.

8 A.M.	Albumen.....	1785	Water.....	9620
1 P.M.	“	1530	“	8900
5 P.M.	“	1500	“	9050
10 P.M.	“	“	6525
Total	“	4815	“	34095

EGESTA.

Kidneys.

Whole quantity of urine 21592·87.

Water.....	20907·63
Solids.....	685·24
Urea.....	340·29
Uric acid	15·31
Chlorine	2·12
Sulphuric acid.....	8·36
Phosphoric acid.....	9·15
Residue.....	310·01

Intestines.

Whole quantity of feces 10257·30.

Water.....	9692·90
Solids.....	565·10
Ether extract.....	10·46
Alcohol extract.....	182·63
Water extract.....	530·5
Insoluble residue.....	318·96

Skin and Lungs.

Total loss through these sources 15319·83.

At 7 A.M. my pulse was 94, at 2 P.M. 98, and at 10 P.M. 98.—
Mean 96·66.

The temperature of the body at the same hours was respectively 96·5°, 97·5°, and 98°.—Mean 97·33°.

At 3 P.M. I abstracted 1330 grains of blood from the median basilic vein. An analysis yielded the following results:—

1000 parts of serum—	1000 parts of blood—
Water..... 900·09	Water..... 773·43
Solids..... 99·91	Solids..... 226·55
Albumen..... 83·21	Fibrin..... 3·18
Extractive..... 12·57	Blood corpuscles.... 137·10
Soluble salts..... 3·12	Albumen..... 71·50
	Extractive..... 11·29
	Soluble salts..... 2·14
	225·21
	Difference..... 1·34
The whole quantity of inorganic salts in 1000 parts of serum was 4·38.	The whole quantity of inorganic salts in 1000 parts of blood was 3·90:
	1000 parts of defibrinated blood contained ·74 of fat.

My weight at the termination of the twenty-four hours was 221·96 pounds; being a loss from the preceeding day of 1·37 pound, or 9590 grains. Of this amount 1330 are accounted for by the blood abstracted for analysis, leaving 8260 as the loss by the excretions.

The mean height of the barometer was 28·503 inches, of the thermometer 45·66°.

The diarrhœa continued on this day with increased violence. I had eight evaenations of the same character as on the previous day. There was very little muens contained in them, and no blood. A microscopical examination revealed the presence of cylindrical and scaly epithelium in considerable quantity.

The debility on this day was extreme, and I was obliged to lie down the greater portion of it. The intellectual faeulties were somewhat confused. My sleep was restless.

The urine contained a large amount of albumen.

The investigations into the value and effects of albumen were now coneluded. In a few days, under a proper dict, I began to recover my usnal health. The diarrhœa ceased spontaneously on the third day. The albumen disappeared from the urine the second day after the termination of the experiments.

The results of the foregoing researches are contained in the accompanying consolidated table.

TABLE II.

	1st day.	2d day.	3d day.	4th day.	5th day.	6th day.	7th day.	8th day.	9th day.	10th day.	Total.	Mean.
INGESTA.												
Albumen.....	87.2)	86.53	113.85	127.5	66.80	69.20	108.00	75.75	61.50	48.15	53.432	89.43-20
Water.....	23.58	24.73	22.55	24.15	24.50	22.50	22.75	25.75	19.10	34.05	23.088	24.58-80
TOTAL.....	321.87	334.28	345.20	389.90	312.30	293.90	346.85	332.80	270.00	38.10	329.420	329.42-00
EGESTA.												
Kidneys—												
Whole quantity of urine.....	16520-36	16837-62	18428-60	17483-75	18128-50	17539-24	16592-83	21235-18	12325-10	21592-87	177385-05	17738-50
Water.....	15363-07	15687-44	17020-02	15654-88	17609-08	16651-88	15911-08	20407-36	11674-86	20907-63	167106-27	16910-62
Solids.....	1157-29	1250-18	1389-58	1429-50	1089-42	978-36	581-75	827-22	650-24	685-24	6588-78	998-97
Urea.....	812-16	922-39	1162-39	1251-32	721-26	728-54	390-00	49-30	329-75	349-24	7130-90	713-09
Uric acid.....	21-39	22-47	28-92	27-40	18-40	24-17	11-28	18-40	14-81	16-31	207-64	207-6
Choline.....	30-54	21-54	10-45	5-37	5-01	4-22	3-61	3-35	2-39	2-12	88-60	8-86
Sulphuric acid.....	28-05	22-05	29-18	21-18	15-12	12-18	10-73	11-24	8-93	8-30	169-25	16-92
Phosphoric acid.....	36-17	34-17	48-21	22-29	17-25	18-45	13-17	11-08	10-52	9-15	220-47	22-04
Residue.....	228-58	225-06	110-42	101-94	292-38	175-80	152-36	290-86	283-80	310-01	2151-91	215-19
Intestines—												
Whole quantity of feces.....	1251-70	1353-69	1428-17	1827-16	1720-54	1852-15	3276-40	3684-02	8729-50	10257-30	35583-63	3558-36
Water.....	943-91	1070-94	1273-91	1386-73	1579-30	1-31-34	2122-00	2273-10	8100-35	9092-90	26683-58	2668-35
Solids.....	308-29	282-75	354-26	437-43	347-24	520-31	1153-80	1310-92	620-15	646-10	5900-25	590-02
Ether extract.....	20-55	18-20	12-40	10-36	17-20	10-42	11-02	8-01	11-24	10-46	136-55	13-65
Alcohol extract.....	89-74	75-32	68-27	80-29	167-52	112-16	100-65	105-27	162-95	182-63	1143-80	114-38
Water extract.....	123-18	124-10	99-68	151-47	85-68	136-58	75-10	122-53	50-17	53-05	1023-54	102-35
Insoluble residue.....	67-23	71-13	172-91	195-31	76-75	261-15	955-13	1075-11	395-79	318-96	3589-47	358-94
Skin and Lungs—												
Total loss from.....	13050-14	15550-69	15803-23	16329-09	13394-96	12927-61	17476-77	12770-80	10018-40	16319-83	144756-52	14475-65
Total egesta.....	32831-20	33848-00	35060-00	36190-00	33900-00	32310-00	37385-90	37690-00	31070-00	47170-00	358414-20	358414-2
Variation in weight.....	-444-20	-420-00	+560-00	+700-00	-2730-00	-3010-00	-2800-00	-4410-00	-7980-00	-5230-00	-2890-20	-2899-42
Pulse.....	84	86-33	87-66	91-33	95-66	92-66	94-00	90-66	90-33	90-66	91-83
Temperature of body.....	97-39°	98°	98°	98-83°	97-16°	97°	97-39°	96-50°	96-50°	97-39°	97-39°
Barometer.....	29-277	29-008	29-245	29-230	29-207	29-110	29-106	29-289	29-235	28-563	29-139
Thermometer.....	45°	42.5, 0°	44°	47-60°	42-33°	42°	35-33°	35-33°	24-33°	45-00°	40-41°

Upon a consideration of the results of the foregoing investigations, and comparing them as far as possible with those obtained while I was living on a normal and ordinary diet, it is seen that the following effects in the mean ensued:—

KIDNEYS.—The *whole quantity of urine* was lessened, as were also the absolute amounts of *water* and *solids*. Relatively, the solids were increased in quantity. The urine was, therefore, more concentrated.

The quantity of *urea* was increased, though not so much so in the mean as was to have been anticipated.

The amount of *uric acid* eliminated was very much increased.

The proportion of *chlorine* was greatly reduced.

The *sulphuric* and *phosphoric acids* were lessened in quantity.

The *residue* was increased in amount.

INTESTINES.—The *whole quantity of feces* was augmented. This result was entirely due to the diarrhœa of the 9th and 10th days. More than half of the whole amount of feces was passed on these days. Throwing them out of the calculation, and it is seen that the mean quantity of feces for the remaining eight days was less than the mean of the five days of the standard series.

The *water* of the feces was greatly increased. This was owing to the same cause as the augmentation of the whole quantity of feces.

The *solids* were reduced in amount.

The *ether extract* was much lessened. It is seen, however, that there was a considerable quantity, notwithstanding no fat was ingested.

The *alcohol extract* was rendered greater in amount.

The *water extract* was diminished in quantity.

The *insoluble residue* was increased.

SKIN AND LUNGS.—No comparison of the losses from these channels during the two series of investigations can be made; as, in the first series, they were not determined. It is perceived,

however, that the general effect of increasing the amount of albumen ingested was to augment the proportion of loss from these sources.

The *weight of the body* is seen in the mean to have materially declined.

The *pulse* was increased in frequency.

The *temperature of the body* was slightly reduced.

The effects of an exclusively albuminous diet upon the constitution of the *blood* will be more clearly perceived from the following table of the first and tenth days' analysis:—

TABLE III.

1000 parts of serum—	1st day.	10th day.	1000 parts of blood—	1st day.	10th day.
Water.....	906.28	900.00	Water.....	776.45	773.43
Solids.....	93.72	99.91	Solids.....	223.55	226.55
Albumen.....	78.28	83.21	Fibrin.....	2.65	3.18
Extractive.....	6.03	12.57	Blood corpuscles.....	142.09	137.10
Soluble salts.....	8.34	3.12	Albumen.....	67.00	71.50
			Extractive.....	5.11	11.29
Whole quant. inorg. salts...	10.29	4.38	Soluble salts.....	6.37	2.14
			Whole quant. inorg. salts...	7.93	3.90
			Fat in 1000 parts defi- } brinated blood	2.39	.74

From this table it is perceived that under the diet of albumen, the *water*, *soluble* and *whole quantity* of *inorganic salts* of the *serum* were diminished, and the *solids*, *albumen*, and *extractive* increased in quantity. In the *whole blood* there was a diminution of the *water*, *blood corpuscles*, *soluble* and *total amount* of *inorganic salts*, and *fat*, while there was an augmentation of the *solids*, *fibrin*, *albumen*, and *extractive*.

The main results of the foregoing investigations I propose to consider more at length under the following heads:—

1. The capability of the digestive organs to dissolve and the absorbents to assimilate a sufficient quantity of albumen to support the calorific process.

2. The relation which the nitrogen of the urea and uric acid exerted bears to the amount absorbed with the albumen.

In relation to the first head, physiologists are not disposed to accord a high value to albumen as an article of respiratory food. The elementary analysis of albumen shows that it does not contain all those substances which enter into the composition of the tissues of the body. It cannot, therefore, of itself, support life or health; and the functional derangements which attended its use during the foregoing investigations abundantly establish this fact. I am very far, therefore, from claiming for it any such power. Nevertheless, I think it is fully proven that before the general health becomes injured by a too long exclusive use of albumen, enough of this substance can be assimilated to repair the waste of the tissues, and support the respiratory function.

According to Liebig,* an adult man daily consumes $13\frac{9}{10}$ ounces (a little over 6000 grains) of carbon, which passes from the system by the lungs and skin as carbonic acid gas. Scharling† states, as the result of his researches, that a powerful adult man exhales from the lungs 867 grammes (about 13,438 grains) of carbonic acid daily. This quantity of carbonic acid is equivalent to 3664.90 grains of carbon. According to Andral and Gavarret,‡ a man twenty-six years of age exhales daily 4065 grains of carbon. Carpenter§ is of the opinion that 3840 grains is the average daily amount of carbon given off through the lungs of a well-grown adult man.

From a series of researches instituted upon myself, with the object of ascertaining the effects of alcohol and tobacco upon the human system, I found that an average of 11674.98 grains of carbonic acid (equivalent to 3185.44 grains of carbon) were daily

* Letters on Chemistry, p. 315, Lond. ed

† Lehmann's Physiological Chemistry, vol. ii. p. 434, Amer. ed.

‡ Quoted in Carpenter's Physiology, p. 526.

§ Physiology, p. 526.

exhaled from the lungs. The method of determination was, however, imperfect, and the absolute amount was doubtless greater than is stated.

The preceding experiments with albumen show that on the first and second days of the series the body slightly decreased in weight, and that on the third and fourth days a small increase ensued. On these days, the quantity of albumen ingested was greater than on the first two days; and that an increased amount was assimilated is evident from the comparatively small quantities of water extract and insoluble residue obtained from the feces. The fact that the bowels were regularly evacuated, shows that the increase of weight observed was not due to any obstruction of the intestinal canal, and consequent accumulation of matter in that channel. Besides the above facts, the great increase in the amount of urea eliminated by the kidneys on the days referred to is also indicative of an augmented assimilation of albumen.

On the fifth day, the body commenced rapidly to lose weight. The effects of so exclusive a regimen began to act injuriously upon the system, while febrile excitement, and other symptoms indicative of derangement of the health, were present; and on the seventh day, notwithstanding a great increase in the quantity of albumen ingested, a loss of weight to the extent of 2800 grains occurred. Albumen appeared in the urine on this day, and of the amount taken into the stomach, over 1000 grains were recovered from the excrement. The loss from the skin and lungs was unusually great.

The following table, showing the amount of albumen daily absorbed into the system from the intestinal canal, and the quantity of carbon entering into its composition, will serve to place the subject in a more evident light. The proportion of assimilated albumen is found by deducting the collective amount of water extract and insoluble residue of the feces from the total quantity of albumen ingested. In the estimation of the carbon contained

therein, I have adopted the analysis of Dumas and Cahours,* of the albumen derived from the serum of beef's blood.

TABLE IV.

	1st day.	2d day.	3d day.	4th day.	5th day.	6th day.	7th day.	8th day.	9th day.	10th day.
Absorbed albumen	8536.59	8455.77	11012.41	12318.22	6517.57	5622.27	9769.76	6377.36	3704.04	4442.99
Absorbed carbon	4559.53	4515.37	5860.62	6577.92	3480.38	3002.29	5118.05	3406.51	3045.95	2372.53

Absorbed albumen.—Mean, 7895.69.

Absorbed carbon.—Mean, 4216.30.

According to the above table, on only one day (the 4th) did the amount of absorbed carbon equal the wants of the system, if we accept Liebig's estimate of the quantity ordinarily given off by the skin and lungs. On the 3d day, the proportion of carbon entering the system did not fall much below Liebig's standard. On these two days only (as we have seen) did the body gain weight. On all the remaining days except the 7th—and on this day it was nearly 900 grains less than Liebig's estimate calls for—the quantity of the absorbed carbon was much below the requirements of the organism, and in the mean was 1800 grains less than the average amount excreted through the skin and lungs, as stated by Liebig.

Leaving, however, all deductions based upon the estimates of others, the broad fact appears that on the 3d and 4th days of the foregoing researches not only was enough albumen assimilated to compensate for the total loss from the excretions, but new matter was deposited in quite an appreciable amount. On the 3d day, too, the temperature of the body was fully up to the natural standard, and on the 4th, very materially exceeded it. Without entering further into the details of this point, I think the conclusion is fully supported that the digestive organs can

* Violette et Archambault, Dictionnaire des Analyses Chimiques, p. 62.

dissolve enough albumen to supply the system with the necessary amount of carbon. If the albumen ingested during these experiments had been conjoined with such mineral substances, in such quantities as the blood and tissues require, in order that nutrition may be perfect, it would doubtless have been better borne by the system, and could have been taken in much larger quantities. Under such circumstances, no good reason can be given why albumen should not have answered all the purposes of plastic formations, and at the same time have sustained the heat-producing function at the proper degree of action.

Whether the opinion of Bidder and Schmidt,* that the gastric juice is not secreted in sufficient quantity to dissolve and metamorphose the necessary amount of albumen for the above purposes, and that the intestinal juice† is equally as important an agent in effecting these changes, or whether the view of Frerichs and Lehmann,‡ who could discover no such power in the latter fluid, be correct, did not come within the range of these investigations to determine. Contrary, however, to Boussingault's§ conclusions, based upon his experiments on ducks, and to the indorsement of his view by Lehmann,|| I think the deduction drawn from the present researches is fully supported by the direct results obtained—at least so far as regards man, whose physiology it is of the greatest importance thoroughly to understand.

2d. The relation which the nitrogen of the urea and uric acid excreted bears to the amount absorbed with the albumen.

The relation which the nitrogen excreted by the kidneys has to that taken into the system with the food is far from being definitely determined, notwithstanding the numerous experiments made with the object of settling the point.

* Die Verdauungssaefte und der Stoffwechsel.—Vom Magensaefte, p. 29.

† Op. cit.—Vom Darmsaefte, p. 260.

‡ Physiological Chemistry, vol. i. p. 510.

§ Mémoires de Chimie Agricole et de Physiologie, pp. 235, 236.

|| Physiological Chemistry, vol. ii. p. 495, Am. ed.

Two views in regard to the origin of urea are held by those who have investigated the subject: one party, of which Lehmann, Frerichs, and Bidder and Schmidt are specially to be mentioned, maintaining that it is derived both from the decomposition of the tissues of the body and from the oxidation of the albuminates taken as food; while the other, of which Liebig and Bischof are the heads, claiming that it is solely derived from the former source.

Whether nitrogenous food is first converted into tissue before its elimination as urea, or whether it undergoes oxidation into this substance while still in the blood, it would seem impossible in the present state of our knowledge to decide. The foregoing investigations, while they cannot be considered as determining this point, afford some very striking results, and throw some additional light upon the subject.

The following table exhibits, for each day of the series, the proportion of nitrogen in the absorbed albumen, the amount excreted with the urea and uric acid, and the ratio which the nitrogen contained in these substances bore to 100 parts of the quantity which was taken into the organism.

TABLE V.

	1st day.	2d day.	3d day.	4th day.	5th day.	6th day.	7th day.	8th day.	9th day.	10th day.
Absorbed nitrogen }	1340.24	1311.55	1728.94	1933.86	1023.25	882.69	1533.85	1001.24	905.53	697.54
Excreted with urea }	378.95	430.38	542.37	583.86	336.53	340.67	182.24	385.98	153.87	314.58
Excreted with uric acid }	7.13	7.49	9.64	9.13	6.13	9.72	3.76	6.16	4.93	5.10
Total.....	386.08	437.87	552.01	592.99	342.66	350.39	186.00	392.14	158.80	319.68
Excreted for each 100 parts absorbed }	29.55	33.38	32.50	30.66	33.48	39.69	12.12	39.16	17.53	45.81

Absorbed nitrogen.—Mean, 1235.87.

Excreted with urea.—Mean, 364.94.

Excreted with uric acid.—Mean, 6.91.

Excreted for each 100 parts absorbed.—Mean, 30.08.

Total, 371.85.

From the foregoing table it is seen that the greatest proportional elimination of nitrogen, in the form of urea and uric acid, occurred on the 6th, 8th, and 10th days, and the smallest on the 7th and 9th. In the mean, 30.08 parts per 100 taken into the system, appeared again in the urine as urea and uric acid.

This result certainly varies greatly from those obtained by any other observer to whose investigations I have had the opportunity of referring. The experiments of Rigg* and of Barral† gave results most nearly in accordance with my own, but there is still a wide difference. The former of these physiologists found that for every 100 parts of absorbed nitrogen, 50.8 were excreted in the urine; the latter, for 100 parts of nitrogen entering the system, found 42.07 in this excretion.

Other physiologists have arrived at results yet more at variance with mine. Lehmann‡ found that while living on a purely animal diet, five-sixths of the nitrogen taken into the system was given off again by the kidneys. Bidder and Schmidt§ found that in a cat, which in twenty-four hours absorbed 8.604 grammes of nitrogen, 7.786 grammes appeared in the urine. Bischof|| (among other examples) found that of 54.09 grammes of nitrogen entering the system of a dog, 29.45 grammes were contained in the excreted urea. It is true, Boussingault¶ recovered from the urine but 37.8 grammes of nitrogen of 139.4 contained in the food of twenty-four hours of a horse, but the excess was in this instance discharged as a constituent of the feces.

In the present experiments, but a small portion of nitrogen could have been discharged by the urine as a constituent of other substances than urea or uric acid. The amount of residue, whose

* Lehmann's Physiological Chemistry, vol. ii. pp. 497, 498.

† Ibid.

‡ Ibid.

§ Die Verdauungssaefte und der Stoffwechsel. Tab. v. s. 306.

|| Der Harnstoff als Maas des Stoffwechsels, s. 65.

¶ Mémoires de Chimie Agricole et de Physiologie, p. 15, et seq.

exact composition was undetermined, was never very large till toward the last, and although albumen was discovered in the urine after the sixth day, the quantity was not such as to make much difference in the proportions given in Table V. The amount of nitrogen eliminated by the feces was of course very small. (It is to be recollected in this connection that in estimating the quantity of albumen entering the organism, the unassimilated residue found in the feces is deducted from the gross amount ingested.)

69.92 grains of nitrogen in every 100 entering the circulation were excreted from the system under some other form than as urea or uric acid, or that proportion formed new combinations, and was retained within the organism. It is difficult to perceive how this enormous amount could have been given off by the lungs and skin, especially as the most exact observations upon animals have determined the loss of nitrogen through these channels to be exceedingly small.

Frequently, during each day of the investigations, I held a glass rod, previously dipped in hydrochloric acid, in the current of the expired air, and, though the white fumes of chloride of ammonium were sometimes produced, this was very seldom, and never in any considerable amount. The skin, during the experiments, had no ammoniacal odor, which would have been present if ammonia in any quantity had been given off.

In view of these facts, I cannot think that the excess of nitrogen escaped from the system as ammonia.

The only conclusion remaining is that the greater part of the absorbed nitrogen continued in the organism either as albumen or under the form of other combinations. The decrease of weight in the body, which occurred on every day but the third and fourth, was doubtless mainly owing to the oxidation of a portion of the fat, and is not incompatible with the formation of new matter of an entirely different character.

On a reference to Table III., it is seen that the nitrogenous matters of the blood (fibrin, albumen, and extractive) were very materially augmented in quantity, and that the fat was greatly diminished. These facts constitute a strong additional argument in favor of the supposition advanced above, and tend to support the view of Bisehof,* that the albuminates of the blood must pass through other processes before they can, merely by the action of oxygen, undergo metamorphosis into urea.

In view of these circumstances, I am disposed to conclude :—

1st. That the proportion of nitrogen eliminated by the kidneys to that absorbed into the circulation is, in man, much less than is generally supposed.

2d. That even when the body is losing weight from the oxidation of its fat, the excess of nitrogen over that escaping by the kidneys is retained in the system, both in its original form and under that of other combinations.

One of the most important results of the foregoing experiments was the discovery of the presence of albumen in the urine. This it is seen was not made until the seventh day, from which time this substance was not absent during the researches; and subsequent observations showed that it was a constituent of the excretions for four days after the conclusion of the series.

The fact that albumen is found in the urine has been before noticed in other connections than as associated with granular degeneration of the kidneys. Professor Walshe† is of opinion that it may occur from other diseases, and from the use of certain articles of food. Begbie‡ states that it may be present in the urine of perfectly healthy persons, in certain conditions of the system, (as pregnancy,) in certain acute and inflammatory diseases, after eating particular kinds of food, (as pastry,) after certain rem-

* Der Harnstoff als Maass des Stoffwechsels, s. 141.

† London Lancet, 1849, p. 416.

‡ British and Foreign Medico-Chirurg. Review, July, 1853, p. 46.

edies, (as juniper,) and after the application of blisters. Bernard* mentions the case of a man who, after eating a large number of raw eggs after fasting, had albumen present in his urine. Bernard, however, is of opinion that it is only under such conditions, viz., an empty state of the digestive organs, and the sudden ingestion of a large quantity of albuminous food, that such an event can ensue, and Rees† denies entirely that this substance is ever found in the urine as the result of an albuminous diet.

The present researches show that albuminuria is produced by the continued use of highly albuminous food in large quantities, and that it was not (so to speak) until the system was saturated with albumen that it made its appearance in the urine.

Without stopping to discuss the other points of these experiments, I proceed to detail the results of the second series, with starch.

II.

STARCH.

The amylaceous substances were, until recently, regarded as being peculiar to vegetable bodies, and the fact of a being presenting distinct evidences of containing them, was sufficient to deny it all claim to an animal existence. This distinctive test, however, can no longer be relied upon. C. Schmidt first showed that cellulose (a substance isomeric with starch) existed as a constituent of the mantle of certain of the tunicata. Gottlieb discovered paramylon (also isomeric with starch) in the body of the infusorium (') *Euglena viridis*; and other observers, among whom

* Leçons de Physiologie expérimentale. Cours de semestre d'hivers, 1854-1855.

† London Medical Gazette, vol. xiii. 1851, p. 49.

Kölliker, Lœwig, Schacht, and Huxley* are to be mentioned, have fully demonstrated the truth of Schmidt's discovery.

Within a short period, Virchow† has carried the investigation still further, and has shown that the corpora amylacea of the human brain are composed of cellulose, and that this substance is also met with in other parts of the body as the result of a certain diseased condition, which he designates as amyloid degeneration.

Busk,‡ however, who has examined this subject very attentively, is of the opinion that the corpuseles in the brain, designated as cellulose by Virchow, are in fact starch, "possessing all the structural, chemical, and optical characters of this substance, as it occurs in plants." It may, therefore, be assumed as a physiological truth that amylaceous substances are not peculiar to vegetables, but are also constituents of the bodies of man and other animals.

From the fact that starch contains no nitrogen in its composition, it cannot contribute to the nutrition of the tissues. Its value, therefore, is generally regarded as resting solely on its heat-producing power. In this respect, its easy digestibility renders it superior to fatty substances, although the latter contain a greater proportion of combustible material. Boussingault§ fed a duck exclusively upon bacon, and found that enough was not assimilated in a given time to repair the loss through the respiratory process. Another duck, fed upon starch, absorbed nearly twice as much as was sufficient to furnish carbon for the wants of the system.

With regard to the process by which starch is digested, much

* For translations of Schacht's and Virchow's papers, and Huxley's original article, see *Quarterly Journal of Microscopical Science*, Nos. 1, 2, 6, 12, and 14.

† Ibid.

‡ *Quarterly Journal of Microscopical Science*, No. 6, p. 115.

§ *Mémoires de Chimie Agricole et de Physiologie*, p. 230.

light has been afforded by the labors of recent investigators. Leuchs first established the fact that the saliva possesses the property of changing starch into sugar. Bidder and Schmidt* state, as the result of numerous experiments, that when the saliva of adult men was mixed with a solution of starch, the conversion into sugar began instantaneously. They also show that other juices, and certain tissues of animals, possess the faculty of effecting this metamorphosis.

On the other hand, Bernard,† while believing that the saliva, under favorable circumstances, out of the body, is capable of transforming starch into sugar, denies it this power within the system, by reason of the short time it is in contact with the food in the mouth, and the fact that the metamorphosis in the stomach is entirely prevented by the gastric juice. He is of opinion that the change of starch into sugar is almost solely due to the action of the pancreatic and intestinal juices.

Mialhé‡ combats these views of Bernard, and while admitting that the conversion of starch into glucose, initiated by the saliva, may be arrested in the stomach by the acid of the gastric juice, contends that the former fluid exercises a very powerful influence in effecting the transformation.

Some recent experiments of Professor F. G. Smith,§ of Philadelphia, would seem to determine this point. Prof. Smith found, in the case of Alexis St. Martin, (the individual upon whom Dr. Beaumont's experiments were instituted,) that after eating farinaceous food, sugar was invariably discovered in the contents of the stomach, and concludes "that the human gastric juice does not prevent the conversion of starch into grape sugar, and that

* Die Verdauungssäfte und der Stoffwechsel. S. 17.

† Leçons de Physiologie expérimentale. Cours de semestre d'été. 1855, p. 155, et seq.

‡ Chimie appliquée à la Physiologie, etc., p. 38, et seq.

§ Medical Examiner, September, 1856, p. 513, et seq.

this change may take place in the stomach independently of the action of the saliva." His investigations appear to have been conducted with great care, and I shall therefore adopt his conclusions.

The change which is commenced by admixture of the amylaceous food with the saliva in the mouth, is continued in the stomach, by the quantity of this secretion swallowed with the aliment. The gastric, pancreatic, and intestinal juices, especially the second named, assist in the process, and eventually, through the combined influence of these several secretions, the starch is brought into a fit form for assimilation. The greater part is absorbed into the circulation as grape sugar, a portion undergoes continued metamorphosis into lactic and butyric acids, and occasionally another part, which has escaped alteration, is discharged with the alvine dejections.

Such is a very condensed outline of some of the principal points of interest connected with the substance under consideration. I now proceed to state my own investigations.

The starch used in these experiments was of the form generally known as corn-starch, and being manufactured for table use, was of a purer quality than the ordinary article. It was always cooked before ingestion, but was taken free from any other substance than the necessary amount of water. The figures in the following pages expressive of the quantity of starch ingested refer to the dry substance before it was cooked; those relating to the amount of water refer both to that portion of this liquid taken with the starch and the quantity drank. The water used was either distilled or snow or rain water.

The investigations were performed under the same conditions (other than the food) as the former series, and as stated at length in the introduction. Such deviations from the standard course as were unavoidable are specially noted. The researches continued ten days.

Thirty days elapsed from the conclusion of the experiments with albumen till the commencement of the present series. In that time my health had entirely recovered, and the weight of the body had undergone a small but steady increase.

At the end of the twenty-four hours immediately preceding the commencement of the following researches, my weight was 224·87 pounds.

FIRST DAY.

INGESTA.

8 A.M.	Starch.....	3000	Water.....	8550
1 P.M.	“	4000	“	8500
5 P.M.	“	2500	“	7450
Total	“	9500	“	24500

EGESTA.

Kidneys.

Whole quantity of urine 14339·51.

Water.....	13588·69
Solids.....	750·82
Urea.....	421·57
Uric acid.....	6·34
Chlorine	85·26
Sulphuric acid.....	30·45
Phosphoric acid.....	27·18
Residue.....	180·02

Intestines.

Whole quantity of feces 1041·86.

Water.....	816·96
Solids.....	224·90
Ether extract.....	49·72
Alcohol extract	50·29
Water extract.....	30·18
Insoluble residue.....	94·71

Skin and Lungs.

Total loss through these channels 19798·34.

My pulse at 7 A.M. was 80, at 2 P.M. 82, and at 10 P.M. 84.—Mean 82.

The temperature of the body at the above hours was respectively 98°, 97·5°, and 97°.—Mean 97·50°.

At 3 P.M. I abstracted 1480·29 grains of blood from the median basilic vein. The following is the analysis:—

1000 parts of serum—	1000 parts of blood—
Water..... 907·34	Water..... 779·33
Solids..... 92·66	Solids..... 220·77
Albumen..... 75·02	Fibrin 1·99
Extractive..... 6·18	Blood corpuscles... 141·18
Soluble salts 10·72	Albumen 63·66
	Extractive..... .. 4·84
	Soluble salts 9·31
	220·98
	Difference..... ·21
The whole quantity of inorganic salts in 1000 parts of serum was 11·98.	The whole quantity of inorganic salts in 1000 parts of blood was 10·42. In 1000 parts of defibrinated blood was 1·83 of fat.

The weight of the body at the end of the twenty-four hours was 224·49 pounds; being a loss of ·38 pound, or 2660 grains; of which 1480·29 are represented by the amount of blood drawn for examination, leaving 1179·71 as the excess of loss from the excretions.

The mean height of the barometer for the twenty-four hours was 29·276 inches, and of the thermometer 1·66°.

On this day I had no abnormal symptoms of any kind. My appetite was very good, and the starch was relished as a pleasant article of food. At night slept well. I took but very little physical exercise on this day, owing to the extreme coldness of the weather.

SECOND DAY.

INGESTA.

8 A.M.	Starch.....	3000	Water.....	6250
1 P.M.	"	3500	"	10000
5 P.M.	"	4000	"	10000
Total	"	10500	"	26250

EGESTA.

Kidneys.

Whole quantity of urine 14970·83.

Water.....	14327·62
Solids.....	643·21
Urea.....	369·15
Uric acid.....	5·42
Chlorine....	31·04
Sulphuric acid.....	19·68
Phosphoric acid.....	25·97
Residue.....	183·95

Intestines.

Whole quantity of feces 1076·53.

Water.....	858·18
Solids.....	218·35
Ether extract.....	51·36
Alcohol extract.....	39·12
Water extract.....	24·39
Insoluble residue.....	103·48

Skin and Lungs.

Total loss through these channels 21122·64.

My pulse was at 7 A.M. 83, at 2 P.M. 85, and at 10 P.M. 84.—
Mean 84.

At the same periods the temperature of the body was respectively 98°, 98·5°, and 98°.—Mean 98·16°.

The weight of the body at the end of the twenty-four hours was 224·43 pounds; a loss of ·06 pound, or 420 grains.

The mean height of the barometer was 29·086 inches, and of the thermometer 3°.

No unusual symptoms of any kind occurred. Appetite good, sleep sound and refreshing. At about 9 P.M., through inadvertence, I drank two ounces of hot whisky punch.

THIRD DAY.

INGESTA.

8 A.M.	Starch.....	3300	Water.....	8900
1 P.M.	“	3500	“	9526
5 P.M.	“	4500	“	10500
Total	“	11300	“	28926

EGESTA.

Kidneys.

Whole quantity of urine 19735.24.

Water.....	19296.09
Solids.....	439.15
Urea.....	225.06
Uric acid.....	5.18
Chlorine.....	14.27
Sulphuric acid.....	12.07
Phosphoric acid.....	26.61
Residue.....	155.96

Intestines.

Whole quantity of feces 925.01.

Water.....	724.47
Solids	200.54
Ether extract.....	45.13
Alcohol extract.....	28.74
Water extract.....	35.41
Insoluble residue.....	91.26

Skin and Lungs.

Total loss from these channels 18585.75.

My pulse at 7 A.M. on this day was 82 per minute, at 2 P.M. 84, and at 10 P.M. 85.—Mean 83.66.

The temperature of the body at the same hours was respectively 98°, 98°, and 98.5°.—Mean 98.16°.

My weight at the end of the twenty-four hours was 224.57; showing an increase over the preceding day of .14 pound, or 980 grains.

The mean height of the barometer was 29.213 inches; that of the thermometer was 4.66°.

Notwithstanding the increase of weight, I felt somewhat weak on this day. My appetite was excellent, and the starch was still relished. The urine was of a somewhat darker color than usual. Numerous starch granules were discovered in the feces by the microscope.

FOURTH DAY.

INGESTA.

8 A.M.	Starch.....	3000	Water.....	8500
1 P.M.	“	3500	“	9500
5 P.M.	“	5500	“	11000
Total	“	12000	“	29000

EGESTA.

Kidneys.

Whole quantity of urine 20245·10.

Water.....	19787·10
Solids.....	458
Urea.....	204·29
Uric acid.....	7·53
Chlorine	8·41
Sulphuric acid.....	10·55
Phosphoric acid.....	18·29
Residue..	216·74

Intestines.

Whole quantity of feces 1438·15.

Water.....	1013·08
Solids.....	425·07
Ether extract.....	40·26
Alcohol extract	29·13
Water extract.....	28·64
Insoluble residue.....	327·01

Skin and Lungs.

Total loss through these channels 18476·25.

My pulse at 7 A.M. was 82, at 2 P.M. 84, and at 10 P.M. 84.—
Mean 83·33.

At the same hours the temperature of the body was respectively 98·5°, 99°, and 99°.—Mean 98·83°.

At the termination of the twenty-four hours my weight was 224·79 pounds; an increase over the preceding day of ·12 pound, equivalent to 840 grains.

The mean height of the barometer was 29·366 inches, and of the thermometer 0·66°.

I felt a good deal of debility during this day, my mind was not active, and there was great indisposition to physical exertion. The appetite was good, but, for the first time, there was some little distaste for the starch, and a great desire to mix salt with it. I experienced at intervals during the day a feeling of oppression about the lungs, which was only relieved by a full inspiration; at night had frequent dreams of falling from precipices, and awoke several times with a sudden start. I also noticed that the saliva was unusually thick and ropy. Under the microscope, an extraordinarily large number of epithelial cells and mucus globules were discovered. It was neutral to test paper.

FIFTH DAY.

INGESTA.

8 A.M.	Starch.....	3000	Water.....	8000
1 P.M.	"	3800	"	9000
5 P.M.	"	4000	"	10000
Total	"	10800	"	27000

EGESTA.

Kidneys.

Whole quantity of urine 18275·82.

Water.....	17885·11
Solids.....	390·71
Urea.....	160·47
Uric acid.....	7·26
Chlorine.....	8·03
Sulphuric acid.....	6·70
Phosphoric acid.....	10·55
Residue.....	197·70

Intestines.

Whole quantity of feces 1145·90.

Water.....	937·68
Solids.....	205·22
Ether extract.....	35·78
Alcohol extract	30·65
Water extract.....	20·50
Insoluble residue.....	118·29

Skin and Lungs.

Total loss through these channels 18518·28.

My pulse at 7 A.M. was 85, at 2 P.M. 87, and at 10 P.M. 87.—Mean 86·33.

The temperature of the body at the same hours was respectively, 98·5° 99°, and 99·5°.—Mean 99°.

At the end of the twenty-four hours my weight was 224·77 pounds; showing a loss of ·02 pound, or 140 grains.

The mean height of the barometer was 29·510 inches, and of the thermometer 1°.

On this day I felt exceedingly feeble. The mind was dull, and it required an effort to fix it upon any subject. Scarcely any physical exercise was taken. The feeling of oppression at the chest had increased, and there was a good deal of sighing respiration. At 12 M. and at 4 P.M. had slight palpitation of the heart. There was some pain in the abdomen through the day, and a large quantity of flatus was discharged with the feces. Slept better than on the previous night, but awoke in the morning with a most intense pain over the left supraorbital arch. This was so severe that I was unable to endure it, and I took forty grains of magnesia with almost instantaneous relief; showing that in all probability the headache was caused by acidity of the stomach. The saliva was of the same character as on the previous day. The microscope still showed an unusual amount of epithelial scales and mucus globules. Reaction neutral.

The urine passed, on rising from bed, was of a darker color than at any time previous during this series of experiments. On testing it for sugar, by Trommer's method, (as had been done every day during the investigations,) there was a clear and well-marked precipitate of the suboxide of copper. The fermentation test, and examination with the microscope for the *torula cerevisiæ*, were both subsequently applied with affirmative results.

SIXTH DAY.

INGESTA.

8 A.M.	Starch.....	2500	Water.....	6200
1 P.M.	“	3500	“	9050
5 P.M.	“	4000	“	10000
Total	“	10000	“	25250

EGESTA.

Kidneys.

Whole quantity of urine 15160·06.

Water.....	14631·87
Solids	528·19
Urea.....	176·28
Uric acid.....	8·49
Chlorine.....	6·22
Sulphuric acid	4·12
Phosphoric acid.....	5·64
Residue.....	347·84

Intestines.

Whole quantity of feces 1097.

Water.....	910·47
Solids.....	186·53
Ether extract	29·89
Alcohol extract	34·75
Water extract.....	14·65
Insoluble residue.....	107·24

Skin and Lungs.

Total loss through these channels 18782·94.

The pulse at 7 A.M. was 85 per minute, at 2 P.M. 85, and at 10 P.M. 90.—Mean 87·66.

At the same periods the temperature of the body was respectively 99°, 99°, and 99·5°.—Mean 99·16°.

At the termination of the twenty-four hours my weight was 224·81 pounds; an increase of ·03 pound, or 210 grains.

The mean height of the barometer was 29·426 inches, and of the thermometer 9·33°.

The debility was still present. Notwithstanding the magnesia taken the previous day, there was considerable torpor of the bowels. Mental phenomena unchanged. The skin was hot, and

there was some fever toward night. The oppression at the chest had, in a measure, subsided. The palpitation of the heart, however, still remained, and was very annoying. I was also troubled a good deal with pyrosis. Rested well at night.

All the urine discharged on this day exhibited (with the tests previously employed) undoubted evidences of containing sugar. The saliva was more natural in its character, though of very feeble alkaline reaction.

My friends noticed, by this time, a change in my personal appearance. My countenance was unusually pale, and my lips of a slight bluish tinge; showing deficient aeration of the blood, or an excessive accumulation of carbonaceous matter in the system.

SEVENTH DAY.

INGESTA.

8 A.M.	Starch.....	2500	Water.....	7000
1 P.M.	“	3500	“	8000
5 P.M.	“	3500	“	9300
Total “		9500	“	24300

EGESTA.

Kidneys.

Whole quantity of urine 15282.25.

Water.....	14856.45
Solids.....	425.80
Urea.....	157.05
Uric acid.....	8.86
Chlorine.....	4.74
Sulphuric acid.....	3.81
Phosphoric acid.....	5.70
Residue.....	244.14

Intestines.

Whole quantity of feces 946.17.

Water.....	750.70
Solids.....	195.47
Ether extract.....	33.76
Alcohol extract	34.29
Water extract.....	27.42
Insoluble residue.....	100.

Skin and Lungs.

Total loss by these channels 17921.58.

At 7 A.M. the pulse was 87, at 2 P.M. 89, and at 10 P.M. 93.—Mean 89·66.

At the above hours, the temperature of the body was respectively 98°, 98·5°, and 98·5°.—Mean 98·33°.

At the end of the twenty-four hours the weight of the body was 224·76 pounds; a decrease of ·05 pound, or 350 grains.

The mean height of the barometer was 29·141 inches, that of the thermometer 12·33°.

The palpitation of the heart was very troublesome on this day, as was also the pyrosis. Debility excessive, especially in the muscles of the back. The desire for other food was very great. The starch was by this time exceedingly disagreeable. One or two slight scratches, which I had received on the hand the day before, became painful, and showed a tendency to inflammation and suppuration. Such a thing had never happened to me before; my flesh always healing readily after such injuries. I did not sleep well, was quite feverish during the night, and awoke in the morning with severe headache.

The urine was still saccharine, of a dark-brown color and very acid reaction. Saliva natural.

Numerous starch granules were discovered with the microscope in the feces. This excretion was also very acid in its reaction, and of a dark, almost black color.

EIGHTH DAY.

INGESTA.

8 A.M.	Starch.....	2225	Water.....	5700
1 P.M.	“	2525	“	10000
5 P.M.	“	3500	“	10000
Total	“	8250	“	25700

EGESTA.

Kidneys.

Whole quantity of urine 20130·87.

Water.....	1978·162	
Solids.....	549·25	
Urea.....		185·33
Uric acid.....		7·94
Chlorine.....		4·30
Sulphuric acid.....		3·09
Phosphoric acid.....		5·86
Residue.....		342·73

Intestines.

Whole quantity of feces 900·61.

Water.....	758·88	
Solids.....	141·73	
Ether extract.....		30·13
Alcohol extract.....		25·37
Water extract.....		12·60
Insoluble residue.....		73·63

Skin and Lungs.

Total loss from these channels 14048·52

At 7 A.M. my pulse was 92, at 2 P.M. 94, and at 10 P.M. 94.—
Mean 93·33.

The temperature of the body at the above hours was respectively 98·5°, 99·5°, and 99°.—Mean 99°.

My weight at the end of the twenty-four hours was 224·57 pounds; a loss from the preceding day of ·19 pound, or 1330 grains.

The mean heights of the barometer and thermometer were respectively 29·105 inches and 15·33°.

Violent headache was present during the whole day. The mind was somewhat confused; an almost constant twitching of the left superior eyelid was experienced, and caused me a great deal of annoyance. The oppression of the chest had returned, and was only relieved by frequent, full, and deep inspirations. There were also griping pains in the lower part of the abdomen,

attended with the discharge of much flatus. The pyrosis still continued. Palpitation of the heart less violent and frequent. Several boils made their appearance on various parts of the body.

The urine, when tested, as before mentioned, exhibited the same characteristic signs of the presence of sugar as previously. Reaction strongly acid. Starch granules in the feces.

NINTH DAY.

INGESTA.

8 A.M.	Starch.....	3500	Water.....	7600
1 P.M.	“	3500	“	9500
5 P.M.	“	4500	“	10500
Total	“	11500	“	27650

EGESTA.

Kidneys.

Whole quantity of urine 23352·11.

Water.....	22879·95
Solids.....	472·16
Urea.....	132·58
Uric acid.....	9·47
Chlorine	3·01
Sulphuric acid.....	2·61
Phosphoric acid.....	5·50
Residue.....	318·99

Intestines.

Whole quantity of feces 1256·45.

Water.....	1043·21
Solids.....	213·24
Ether extract	21·36
Alcohol extract	18·51
Water extract.....	15·74
Insoluble residue.....	157·63

Skin and Lungs.

Total loss from these channels 13631·44.

At 7 A.M. on this day my pulse was 90, at 2 P.M. 93, and at 10 P.M. 95.—Mean 92·66.

The temperature of the body at these hours was respectively 99·5° 99·5°, and 100°.—Mean 99·66°

The weight of the body at the end of the twenty-four hours was 224·70 pounds; an increase of ·13 pound, or 910 grains over the previous day.

The mean height of the barometer was 29·252 inches, and of the thermometer 13°.

The symptoms observed on this day did not differ materially from those of the day before. I was obliged, however, from weakness and general indisposition, to go to bed at 8 P.M. Did not sleep well.

The urine was still highly saccharine, and of the same clear brown color as before noticed.

TENTH DAY.

INGESTA.

8 A.M.	Starch.....	2200	Water.....	6000
2 P.M.	"	4525	"	11500
5 P.M.	"	3500	"	9000
Total	"	10225	"	26500

EGESTA.

Kidneys.

Whole quantity of urine 22785.

Water.....	22272·43
Solids.....	512·57
Urea.....	121·77
Uric acid	9·36
Chlorine	1·89
Sulphuric acid.....	2·26
Phosphoric acid.....	5·31
Residue.....	340·59

Intestines.

Whole quantity of feces 1250·27.

Water.....	945·42
Solids.....	204·85
Ether extract.....	25·63
Alcohol extract.....	25·80
Water extract.....	17·43
Insoluble residue.....	135·49

Skin and Lungs.

Total loss through these channels 12599·73.

My pulse at 7 A.M. was 91, at 2 P.M. 90, and at 10 P.M. 93.—
Mean 91·33.

The temperature of the body at the same hours was respectively 99°, 99·5°, and 99·5°.—Mean 99·33°.

At 3 P.M. I abstracted 1350 grains of blood from the median basilic vein, and, upon analysis, found it to be constituted as follows:—

1000 parts of serum—		1000 parts of blood—	
Water.....	920·81	Water.....	796·49
Solids.....	79·19	Solids.....	203·51
<hr/>		<hr/>	
Albumen.....	63·45	Fibrin.....	3·15
Extractive.....	12·35	Blood corpuscles....	132·60
Soluble salts.....	2·12	Albumen.....	55·96
	<hr/>	Extractive.....	11·25
	77·92	Soluble salts.....	1·87
Difference.....	1·27		<hr/>
<hr/>		204·83	
The whole quantity of inorganic salts in 1000 parts of serum was 2·89.		Difference.....	1·32
		<hr/>	
		The whole quantity of inorganic salts in 1000 parts of blood was 2·05.	
		In 1000 parts of defibrinated blood were 2·74 of fat.	

The weight of the body at the end of the twenty-four hours was 224·53 pounds; being a loss of ·18 pound, or 1260 grains. As, however, 1350 grains of blood were taken from the body, there was an actual increase of 90 grains, or, more properly, would have been, but for the loss of blood.

The mean height of the barometer was 29·155 inches, and of the thermometer 12·66°.

The general symptoms observed were of the same character as those of the last two days, but more strongly marked.

The urine was highly saccharine, and of the same brown color; resembling Madeira wine.

The immediate effect of the slight abstraction of blood was to

relieve the feeling of oppression at the chest; but in an hour it returned with increased violence. The debility was very great.

The experiments with starch were now at an end. Immediately on their termination, I ate a hearty breakfast, but my stomach was in so weak and disordered a condition that the food was almost instantly rejected. I found that I was obliged to resume my ordinary diet with some degree of caution. After a few days I became free from all unpleasant symptoms, and rapidly regained my usual good health. It is remarkable, however, that for the first few days after the conclusion of the experiments, I steadily lost weight, so that on the tenth day I weighed but 223·18 pounds. Sugar was detected in the urine till the morning of the sixth day.

The accompanying table embraces the main results of the foregoing investigations:—

TABLE VI.

	1st day.	2d day.	3d day.	4th day.	5th day.	6th day.	7th day.	8th day.	9th day.	10th day.	Total.	Mean.
INGESTA.												
Starch.....	9600	10500	11300	12000	10800	10000	9600	8250	11500	10225	103755	10357.50
Water.....	24500	26250	28925	29000	27000	29250	24500	25700	27650	26500	265076	26507.50
Total.....	34000	36750	40225	41000	37800	39250	35800	33950	39150	36725	368631	36865.10
EGESTA.												
Kidneys—												
Whole quantity of urine.....	14330.51	14970.83	19735.24	20245.10	18275.82	15160.06	15289.25	20130.87	22352.11	22785.00	184276.79	18427.67
Water.....	135885.09	14327.62	19206.09	19787.10	17885.11	14631.87	14850.45	19781.62	22879.96	22272.43	179100.93	17910.09
Solids.....	750.82	643.21	430.15	458.00	390.71	628.19	425.80	540.25	472.16	612.57	6169.86	516.38
Urea.....	421.57	380.15	225.06	204.39	190.47	176.28	157.05	185.32	162.48	121.77	2163.55	215.35
Uric acid.....	6.34	5.42	5.18	7.53	7.26	8.40	8.36	7.94	9.47	9.36	78.35	7.63
Chlorine.....	85.26	31.04	14.27	8.41	8.03	4.74	4.30	3.81	5.01	1.89	167.17	10.71
Sulphuric acid.....	39.45	19.48	12.97	10.55	6.70	4.12	3.70	3.00	2.61	2.26	97.34	9.73
Phosphoric acid.....	27.18	25.67	12.61	18.29	10.55	5.64	5.70	5.85	5.30	5.31	136.67	13.66
Residue.....	180.02	183.35	165.96	216.74	107.70	347.84	244.14	342.73	318.99	340.59	2528.05	252.86
Intestines—												
Whole quantity of feces.....	1041.86	1076.53	925.01	1438.15	1145.90	1007.00	946.17	900.61	1256.45	1250.27	11077.95	1107.80
Water.....	816.96	858.18	724.47	1013.08	997.68	910.47	750.70	758.88	1043.21	945.42	8882.15	886.21
Solids.....	224.90	218.35	200.54	425.07	205.22	186.53	195.47	141.73	213.24	204.85	2215.00	221.59
Ether extract.....	49.72	51.36	45.13	40.26	35.78	29.89	33.76	30.13	21.36	25.03	349.02	30.50
Alcohol extract.....	50.29	39.12	28.74	30.75	30.66	34.75	34.29	25.37	18.51	25.80	316.63	31.66
Water extract.....	30.18	24.80	35.41	28.64	20.50	14.65	27.42	12.60	15.74	17.43	220.96	22.09
Insoluble residue.....	94.71	103.48	91.26	327.01	118.29	107.24	100.00	78.63	157.63	135.49	1309.54	130.95
Skin and Lungs—												
Total loss by these channels.....	19798.34	21122.64	18585.75	18476.25	18518.28	18782.94	17921.58	14248.52	13631.44	12590.73	173685.97	17368.59
Total egesta.....	35179.71	37170.00	39245.00	40160.00	37940.00	35040.00	34150.00	35280.00	38240.00	36628.00	369040.71	36904.07
Variation in weight of body.....	—1179.71	—420.00	+860.00	+840.00	—140.00	+210.00	—350.00	—1330.00	+010.00	+90.00	—259.71	—38.97
Pulse.....	82	84	83.66	83.66	86.33	87.66	89.66	93.33	92.66	91.33	87.42	87.42
Temperature of body.....	97.50°	98.16°	98.16°	98.83°	99°	99.16°	98.33°	99°	99.66°	99.83°	98.81	98.81
Barometer.....	29.276	29.086	29.213	29.386	29.510	29.425	29.141	29.165	29.252	29.155	29.235	29.235
Thermometer.....	—1.69°	30	—4.66°	—0.66°	10	9.33°	12.33°	15.33°	13°	12.66°	6.66°	6.66°

A consideration of the foregoing investigations, and comparison of the results with those of the standard series, show that under the use of food consisting only of starch and water, the following effects ensued :—

KIDNEYS.—The whole quantity of urine was lessened, as was also the amount of its solid matter, and that of each constituent, (urea, uric acid, chlorine, and sulphuric and phosphoric acids.) The residue of solid matter remaining after the deduction of the sum of the above named substances was, however, greatly increased.

The diminution in the quantity of urine eliminated was partly due to the fact that there was a less amount of fluids ingested than during the preliminary series, and partly that the food was not of a character to maintain the several solid constituents at their ordinary normal amounts. It was from this latter cause that so great a reduction took place in the quantity of urea, uric acid, chlorine, and sulphuric and phosphoric acids. During the present investigations, these substances must have been entirely derived from the disintegrated tissues of the body; the food containing no matter from which they could have been elaborated.

The increase of solid residue was probably owing to the sugar present, and, perhaps, to some other substance containing a large proportion of carbon. The increased depth of color observed in the urine supports this latter hypothesis. Recent investigations have almost completely established the fact that the coloring matter of the urine is a vehicle for the removal of carbon which has not been eliminated by other channels.*

The fact that sugar was detected in the urine after a few days' use of the starch, is important physiologically, and must have no little bearing upon the pathology of a disease as yet but little understood.

* Bird. Urinary Deposits, p 88.

According to Bernard,* sugar in the animal economy has an internal and external origin, the liver being the organ by which it is formed in the system, and the food furnishing that derived from without. This physiologist is, however, of opinion (and he adduces many striking experiments in support of this theory) that normally the sugar taken into the system with the food, and which enters the portal vein, never reaches the general circulation, but is destroyed by the liver, and transformed into an emulsive substance, possessing none of the chemical or physical characteristics of sugar. The sugar of the food, therefore, is never normally found as a constituent of the urine. To this rule he makes an exception as regards cases of fasting, and the subsequent ingestion of a large quantity of sugar. Then, he states, absorption from the intestines taking place with increasing energy, a great quantity of sugar is thrown upon the liver, and, being more than it is able to transform, the excess passes into the main circulation, and is found in the urine.

The present investigations, it is seen, are entirely opposed to Bernard's doctrine of the perfect destruction of the alimentary sugar by the liver, as it is not probable the sugar found in my urine could have had any other origin than the food which was transformed into this substance in the intestines, and absorbed as such into the circulation.

In obtaining this result, I am not altogether alone. Von Becker has definitely established the fact that the amount of sugar in the blood is influenced by the character of the food; and Uhle and Lehmann found it to appear in the urine of rabbits after the injection of a solution containing it into the blood.

I am disposed to regard the appearance of sugar in the urine, ensuing upon the excessive use of amylaceous food, to be due to

* *Leçons de Physiologie expérimentale. Cours de semestre d'hivers, 1854, 1855.* The reader is referred to this work for Bernard's views in full.

a deficient relative amount of oxygen in the blood. This hypothesis may be more clearly set forth by recalling the facts that before assimilation, the starch taken as food is transformed into dextrin, then into glucose or grape sugar, and is chiefly under this form absorbed into the system. The sugar, after its entrance into the blood-vessels, (provided a sufficient amount of oxygen be brought into chemical contact with it,) is, after undergoing continued metamorphosis, entirely decomposed into carbonic acid and water, and, as such, is eliminated from the pulmonary mucous membrane. A deficiency of oxygen causes a partial interruption of this process, and a portion of the sugar is merely metamorphosed into fat, and under this form remains in the system. A still greater deficiency of oxygen, or, what amounts to the same, a corresponding increase of the quantity of sugar in the blood, would cause a portion of this latter substance entirely to escape metamorphosis, and this portion would make its appearance as a constituent of the urine if augmented beyond a definite amount. In support of this theory are to be adduced the numerous carefully conducted investigations of Dechambre, from which it appears that sugar is constantly to be met with in the urine of the aged as an effect of deficient hematosis. It is well known that the use of feculent food invariably increases the proportion of this substance in diabetic urine.

INTESTINES.—The quantity of feces was reduced, as was also that of each of its constituents determined.

The decrease in the total amount of feces was due to the facts that starch is a substance of easy digestibility, and that no indigestible substances were taken into the system.

The reduction in the amounts of ether, alcohol, and water extracts was also mainly owing to the character of the aliment. As no fat was taken with the food, it would seem that the first of these was present in greater amount than could have been expected, unless we adopt the hypothesis that farinaceous food is

converted into fat in the intestines; to which theory the experiments of Boussingault on ducks are directly at variance.

The weight of the body is seen to have declined altogether 469·71 grains, not counting, in this calculation, the weight of the blood abstracted for analysis. This loss is much less than the drain from the waste of the nitrogenous tissues, and shows that a very considerable amount of new matter must have been deposited within the system. The chemical constitution of starch forbids the idea that this material could have been of a nature to serve for the renovation of the worn-out tissues of the body. It must, on the contrary, have consisted of fat, derived from the metamorphosis of the amylaceous food. The slight loss of weight observed shows, therefore, that the starch was assimilated not only in quantity sufficient for the immediate wants of the system, but also in such an amount as to allow the deposition of fat to such an extent as, within a few grains, to compensate for the total loss through the nitrogenous constituents of the excretions. The actual increase observed in the temperature of the body, and several of the pathological occurrences, also show that there was no deficiency of carbon in the system.

EFFECT UPON THE CONSTITUTION OF THE BLOOD.—The annexed table exhibits the results of the analysis of the blood on the first and tenth days of the experiments.

TABLE VII.

1000 parts of serum—	1st day.	10th day.	1000 parts of blood—	1st day.	10th day.
Water.....	907·34	920·81	Water.....	779·33	796·49
Solids.....	92·66	79·19	Solids.....	220·77	203·51
Albumen.....	75·02	63·45	Fibrin.....	1·99	3·15
Extractive.....	6·18	12·35	Blood-corpuscles.....	141·18	132·60
Soluble s. lts.....	10·72	2·12	Albumen.....	63·66	55·96
			Extractive.....	4·84	11·25
Whole quant. inorg. salts...	11·98	2·89	Soluble salts.....	9·31	1·87
			Whole quant. inorg. salts...	10·42	2·05
			Fat.....	1·83	2·74

From this table it is seen that, in the serum, the water was increased in quantity, and the solids proportionally diminished. The albumen and salts were reduced in amount, while the extractive was very much increased.

In the whole blood, the proportion of water was likewise increased, and that of the solids lessened. The fibrin, extractive, and fat were augmented; the blood corpuscles, albumen, and salts diminished.

Most of these results were to have been anticipated. The most important of them are the increase in the fibrin, extractive, and fat.

So many different views of the value and character of the fibrin of the blood are held by physiologists that I merely state the fact of its occurrence in this fluid in increased amount after farinaceous diet, without attempting to account for it. Whether fibrin is a substance of the ascending or descending grade of metamorphosis, is as yet far from determination.

The increase in the amount of fat is sufficiently accounted for by the character of the food, and might have been anticipated, if the theory given explanatory of the cause of the presence of sugar in the urine be regarded as correct. The diminished amount of fat in the blood after the albuminous diet, and its increase after an amylaceous one, show that the proportion of this substance in the circulating fluid is subject to variation with the character of the ingesta; a circumstance with which the experiments of Boussingault* are at variance.

The increase in the proportion of the extractive was probably due to some carbonaceous substance present in augmented quantity.

Upon the whole, if further evidence of the incapability of starch to sustain for any length of time health or life in the

* Op. cit., p. 281, et seq.

human subject were wanting, the present investigations would appear to furnish it. The value of starch is, however, very great, for, notwithstanding the derangement of the health, both physical and mental, produced by strict adherence to a diet of this substance, it is perceived that but slight loss of weight occurred. This latter fact, resulting as it did from the deposition of fat, is not to be regarded as an entirely normal result. Nevertheless, it is a most valuable indication that farinaceous food fulfils the condition of supplying a sufficiency of carbon to the system.

III.

G U M.

The chemical constitution of gum differs from that of starch only in containing two additional atoms of both hydrogen and oxygen. It is never found as a component part of the bodies of animals, and of the vegetable substances ordinarily used as food by man, few, if any, contain it. It is, however, occasionally employed in the sick-room, from an idea, formerly very prevalent and not yet entirely extinct, that it possesses great nutritive power, and is sometimes met with as an ingredient of certain sweetmeats.

Notwithstanding that it is exceedingly soluble in water, the recorded experiments of several physiologists tend to show that gum is possessed of little or no nutritive value, or capability of supporting respiration, owing to its almost complete indigestibility. Thus Boussingault* fed a duck with fifty grammes of gum-arabic, and found forty-six in the excrements; and Frerichs,

* Mémoires de Chimie agricole et de Physiologie, p. 232.

Blondlot, and Lehmann* found that neither the saliva nor gastric juice exercised any digestive effect upon this substance.

With the object of contributing to the more complete elucidation of the subject, the following investigations were instituted. My original intention was to have continued them, if possible, ten days, as in the former two series; but, owing to the debility and great derangement of health produced, I was obliged, very much to my regret, to discontinue them at the end of the fourth day.

Pure gum-arabic was the article used during these investigations. It was ingested dissolved in water, (the proportion of this liquid entering into its composition having been previously ascertained.) The figures relating to the gum refer to the dry substance, and those indicating the quantity of water to the whole amount of this liquid taken into the stomach uncombined, and with the gum. The water was distilled, or rain-water. No other food was taken.

The conditions of physical and mental exercise, sleep, etc. were as far as possible the same as in the previous series. I was unable, however, to adhere as rigidly to the standard system as I desired. The deviations are noticed in the proper places. Twenty-five days elapsed between the termination of the starch series of investigations and the commencement of the present. At this latter time my health appeared to be very good. At the end of the twenty-four hours immediately preceeding, my weight was 225.33 pounds.

FIRST DAY.

INGESTA.			
8 A.M.	Gum.....	2300	Water..... 9000
1 P.M.	"	3000	"
5 P.M.	"	3000	"
Total	"	8300	"

* Lehmann's Physiological Chemistry, vol. ii. p. 386.

EGESTA.

Kidneys.

Whole quantity of urine 20728·61.

Water.....	20157·03
Solids.....	571·58
Urea.....	330·15
Uric acid.....	7·45
Chlorine.....	46·28
Sulphuric acid.....	21·57
Phosphoric acid.....	24·13
Residue.....	142·

Intestines.

Whole quantity of feces 8529·14.

Water.....	3284·34
Solids.....	5244·80
Ether extract.....	31·55
Alcohol extract.....	30·27
Water extract.....	5030·36
Insoluble residue.....	152·62

Skin and Lungs.

Total loss from these channels 12422·94.

My pulse at 7 A.M. was 80, at 2 P.M. 84, and at 10 P.M. 89.—

Mean 84·33.

At the same hours the temperature of the body was respectively 98·5°, 98°, and 97·5°.—Mean 98°.

At 3 P.M. I took 1359·31 grains of blood from the median basilic vein. This, upon analysis, was found to be constituted as follows:—

1000 parts of serum—

Water	907·43
Solids	92·57

Albumen.....	77·36
Extractive.....	5·15
Soluble salts.....	9·22
	<hr/>
	91·73
Difference.....	·84

The whole quantity of inorganic salts in 1000 parts of serum was 11·01.

1000 parts of blood—

Water	778·04
Solids	221·96

Fibrin.....	2·05
Blood corpuscles....	138·22
Albumen	66·32
Extractive.....	4·08
Soluble salts.....	7·96
	<hr/>
	218·63

Difference 3·33

The whole quantity of inorganic salts in 1000 parts of blood was 10·49; 1000 parts of defibrinated blood contained 2·13 of fat.

The weight of the body at the end of the twenty-four hours was 224·57 pounds; being a loss of ·82 pound, or 5740 grains; of which 1359·31 are to be ascribed to the blood abstracted for analysis, leaving a balance of 4380·69 grains as the actual loss from the excretions.

The mean height of the barometer on this day was 28·324 inches, and of the thermometer 31·33°.

About the middle of this day I felt quite hungry. After eating the gum, at 5 P.M., this feeling subsided, but returned again in the course of the evening. I had severe colicky pains in the lower part of the abdomen after eating the second meal of gum. Had two evacuations from the intestinal canal: one at 9 P.M., and one at 6½ A.M. The feces of both were hard, of a dark-brown color, and of a very strong acid reaction.

SECOND DAY.

INGESTA.

8 A.M.	Gum.....	2150	Water.....	9300
1 P.M.	“	2100	“	10000
5 P.M.	“	3000	“	10050
		<hr/>		<hr/>
Total	“	7250	“	29350

EGESTA.

Kidneys.

Whole quantity of urine 21385·97.

Water.....	20934·74
Solids.....	451·23
Urea.....	301·24
Uric acid.....	8·20
Chlorine.....	21·15
Sulphuric acid.....	12·05
Phosphoric acid.....	13·35
Residue.....	95·24

Intestines.

Whole quantity of feces 9350·28.

Water.....	3975·09
Solids.....	5375·19

Ether extract	17.43
Alcohol extract	12.84
Water extract	5297.62
Insoluble residue	47.20

Skin and Lungs.

Total loss through these channels 11883.75.

At 7 A.M. on this day my pulse was 88, at 2 P.M. 88, and at 10 P.M. 94.—Mean 90.

At the corresponding hours the temperature of the body was respectively 97°, 97.5°, and 97.5°.—Mean 97.33°.

At the termination of the twenty-four hours my weight was 223.65; a loss of .86 pound, or 6020 grains.

The mean height of the barometer was 28.706 inches, and of the thermometer 8°.

The feeling of hunger was very strong on this day, and I experienced a good deal of debility. Both the hunger and weakness became less a short time after eating, but they soon returned. The pains in the abdomen still continued. They became more severe after eating. Two evacuations of the bowels occurred: one at 2½ P.M., the other at 7 P.M. They were both hard, and were of a much lighter color than on the previous day. Reaction strongly acid. At night my sleep was disturbed by unpleasant dreams, and I awoke in the morning with severe headache and high fever.

The saliva was scanty, and of a slight acid reaction to litmus paper.

THIRD DAY.

INGESTA.

8 A.M.	Gum.....	2000	Water.....	10000
1 P.M.	"	2150	"	9890
5 P.M.	"	3150	"	10230
Total	"	7300	"	30120

EGESTA.

Kidneys.

Whole quantity of urine 23721·50.

Water	23334·71
Solids.....	386·79
Urea.....	282·64
Uric acid.....	9·27
Chlorine ..	6·33
Sulphuric acid.....	6·97
Phosphoric acid.....	7·09
Residue.....	74·49

Intestines.

Whole quantity of feces 9783·56.

Water.....	3152·09
Solids.....	6631·47
Ether extract.....	10·72
Alcohol extract.....	9·55
Water extract.....	6581·40
Insoluble residue.....	29·80

Skin and Lungs.

Total loss from these channels 10704·94.

At 7 A.M. my pulse was 104, at 2 P.M. 112, and at 10 P.M. 110.—
Mean 108·66.

At the same hours the temperature of the body was respectively 99·5°, 101°, and 101°.—Mean 100·50°.

At the end of the twenty-four hours my weight was 222·68; showing a loss from the preceding day of ·97 pound, equivalent to 6790 grains.

The mean height of the barometer was 29·264 inches, and of the thermometer 19°.

The debility and hunger were extreme on this day. There was also considerable febrile excitement, attended with heat and dryness of the skin, and headache. I was too much indisposed to read any, and the physical exercise was likewise reduced. In the afternoon, I was obliged to lie down, and at that time slept about one hour.

Three evacuations from the bowels occurred: one at 12 M., one

at 4½ P.M., and one at 7½ P.M. The feces were very solid, and of a light-clay color. I was very much annoyed by the abdominal pains. At night I was restless, and slept but little. In the morning, awoke feverish and unrefreshed.

FOURTH DAY.

INGESTA.

8 A.M.	Gum.....	2000	Water.....	9000
1 P.M.	“	2400	“	9500
5 P.M.	“	2500	“	11500
Total	“	6900	“	30000

EGESTA.

Kidneys.

Whole quantity of urine 20516·31.

Water.....	20163·88
Solids.....	352·43
Urea.....	274·50
Uric acid.....	9·35
Chlorine	3·20
Sulphuric acid.....	3·90
Phosphoric acid.....	4·55
Residue.....	56·93

Intestines.

Whole quantity of feces 10964·73.

Water.....	3529·71
Solids.....	7435·02
Ether extract.....	10·14
Alcohol extract	8·30
Water extract.....	7390·10
Insoluble residue.....	26·48

Skin and Lungs.

Total loss by these channels 12656·45.

At 7 A.M. on this day my pulse was 102, at 2 P.M. 99, and at 10 P.M. 108.—Mean 103.

At the corresponding hours, the temperature of the body was respectively 97·5°, 98°, and 97·5°.—Mean 97·66°.

Perceiving that I should not be able to continue the investigations after this day, I abstracted, at 3 P.M., 1272·51 grains of blood from the median basilic vein. The analysis yielded the following results:—

1000 parts of serum—		1000 parts of blood--	
Water.....	912·84	Water.....	784·35
Solids.....	87·16	Solids.....	215·65
Albumen	72·40	Fibrin.....	2·71
Extractive.....	8·23	Blood corpuscles...	135·64
Soluble salts.....	5·11	Albumen.....	62·20
	85·74	Extractive	7·39
Difference... ..	1·42	Soluble salts.....	4·01
The whole quantity of inorganic salts in 1000 parts of serum was 6·89.			211·95
		Difference.....	3·70
		The whole quantity of inorganic salts in 1000 parts of blood was 6·37 : 1000 parts of defibrinated blood contained 1·80 of fat.	

The weight of the body, at the end of the twenty-four hours, was 221·63 pounds; a loss, therefore, of 1·05 pound, or 7350 grains; of which 1272·51 are accounted for by the blood abstracted, so that there remain 6077·49 grains as the loss by the excretions.

The mean heights of the barometer and thermometer were respectively 29·369 inches and 8°.

The hunger, debility, and febrile excitement were very great on this day; but not more so than on the previous day. The pains in the abdomen were severe, and lasted nearly the whole period of twenty-four hours. There was also some tenderness of the abdomen on pressure. Eating the gum failed now to relieve, even for a short time, the sensation of hunger. Four evacuations occurred from the intestinal canal: one at 11 A.M., one at 3 P.M., one at 9 P.M., and the other at the regular hour. All were

very solid, and of a light-clay color. It required a good deal of straining to eject the feces. I omitted all study on this day, and took but a trifling amount of physical exercise. The greater part of the afternoon was passed in bed. At night I did not sleep at all well.

Fearful of inducing disease if I persevered with the experiments, and also, what was perhaps a more powerful inducement, unable longer to refrain from other food, I discontinued them at the end of this day.

About 4 P.M. of the fifth day from the commencement, I felt great weight and pain in the rectum, but was unable to pass anything at stool. I therefore took an enema of warm water, and in a few minutes ejected a large quantity of hard fecal matter streaked with blood. The water extract of this amounted to 3352.45 grains. No other examination of the excrement was made.

I felt very much indisposed for several days after the conclusion of the researches, but by care, and prudence in diet, no very untoward result ensued.

The results of this series are contained in the accompanying table:—

TABLE VIII.

	1st day.	2d day.	3d day.	4th day.	Total.	Mean.
INGESTA.						
Guin.....	8300	7250	7300	6900	29750	7437.50
Water.....	29000	29350	30120	30000	118470	29617.50
Total.....	37300	36600	37420	36900	148220	37055.00
EGESTA.						
<i>Kidneys—</i>						
Whole quantity of urine.....	20728.61	21385.97	23721.50	20516.31	86152.39	21538.09
Water.....	20157.03	20934.74	23334.71	20163.88	84390.36	21097.59
Solids.....	571.58	451.23	386.79	352.43	1762.03	440.50
Urea.....	330.15	301.24	282.64	274.50	1188.53	297.13
Uric acid.....	7.45	8.20	9.27	9.35	35.27	8.81
Chlorine.....	46.28	21.15	6.33	3.20	76.86	19.21
Sulphuric acid.....	21.57	12.05	6.97	3.90	44.49	11.12
Phosphoric acid.....	24.13	13.35	7.09	4.55	49.12	12.28
Residue.....	142.00	95.24	74.49	56.93	288.66	67.16
<i>Intestines—</i>						
Whole quantity of feces.....	8529.14	9350.28	9783.56	10964.73	38627.73	9656.93
Water.....	3284.34	3975.09	3152.09	3529.71	13941.23	3485.30
Solids.....	5244.80	5375.19	6631.47	7435.02	24686.50	6171.62
Ether extract.....	31.55	17.43	10.72	10.14	79.84	19.96
Alcohol extract.....	30.27	12.84	9.55	8.30	60.96	15.24
Water extract.....	5030.36	5297.62	6551.40	7390.10	24299.48	6074.87
Insoluble residue.....	152.62	47.20	29.80	26.48	255.10	63.71
<i>Skin and Lungs—</i>						
Total loss by these channels.....	12422.94	11883.75	10704.94	11496.45	47668.08	11917.02
Total egesta.....	41880.59	42620.00	44210.00	42977.49	171688.08	42922.02
Variation in weight.....	-4380.69	-6020.00	-6790.00	-6077.49	-23268.18	-5817.04
Pulse.....	84.33	90	108.66	103	96.49
Temperature of body.....	98°	97.33°	100.50°	97.66°	98.37°
Barometer.....	28.324	28.706	29.264	29.369	28.915
Thermometer.....	31.33°	8°	19°	8°	16.58°

In considering these investigations, it is seen that the following effects ensued :—

KIDNEYS.—The whole quantity of urine and the proportion of water were increased; the solids and amounts of each constituent were very much reduced.

INTESTINES.—The whole quantity of feces, the water, solids, and

water extract were enormously increased over the normal average and the means of either of the other series of researches. The ether and alcohol extracts were decreased in quantity.

SKIN AND LUNGS.—The loss from these sources was less than under either the albumen or starch series, and was probably also below the normal extent.

The loss of weight in the body was very great.

The pulse was increased in frequency, as was also the temperature of the body.

The following table shows the alterations induced in the composition of the blood:—

TABLE IX.

1000 parts of serum—	1st day.	4th day.	1000 parts of blood—	1st day.	4th day.
Water.....	907.43	912.84	Water.....	778.04	784.35
Solids.....	92.57	87.16	Solids.....	221.96	215.65
Albumen	77.36	72.46	Fibrin.....	2.05	2.71
Extractive.....	5.15	8.23	Blood corpuscles.....	138.22	135.64
Soluble salts.....	9.22	5.11	Albumen	66.32	62.20
Inorganic salts.....	11.01	6.89	Extractive.....	4.08	7.39
			Inorganic salts	10.40	6.37
			Fat.....	2.13	1.80

From this table it appears that in the serum the proportion of water was augmented, and that of the solids was diminished, and that the albumen and salts were reduced in amount, and the extractive increased. In the whole blood, the same effects ensued with the addition that there was a slight increase in the amount of fibrin, and a decrease in the blood corpuscles and fat.

It is evident from these researches that but little, if any, of the gum taken into the stomach was absorbed into the circulation. In all 29,750 grains of gum were ingested. The water extract of the feces, which consisted almost entirely of gum, amounted during the four days of the investigations to 24,299.48 grains. To this sum should of course be added the water extract obtained

the day after the conclusion of the experiments, (3352·45 grains,) making a total of 27·651·93 grains, which, with the exception of very small quantities of other matters, consisted entirely of gum. A balance of 2098·07 grains remains, but it is probable that a considerable portion, if not the whole of this, was subsequently passed from the bowels, as hard lumps continued to be discharged from this channel for several days.

The great loss of weight (nearly 3·33 pounds) is not surprising after a knowledge of the above facts. Water was always taken in such quantities as desired, or of course the decrease of weight would have been much greater. The fever, hot skin, etc. were indicative of irritation and debility.

If we admit the non-absorption of the gum, the solid constituents of the urine must have been entirely derived from the effete tissues of the body. The amounts of each are therefore probably such as would have been excreted had no food been taken into the stomach. The carbonic acid of the expired air could have had no other source than the oxidation of the fat of the body, which also furnished a portion of the aqueous vapor expired.

The alterations in the proportions of the several constituents of the blood are also doubtless such as would have taken place under inanition. The increase observed in the quantity of extractive and fibrin is important, but may have been accidental.

From these researches I conclude that gum, so far from having any value as an alimentary substance, is positively injurious, owing to the fact of its clogging the intestines, and thus proving a cause of irritation. As an article of food for the sick, its use should be especially condemned.

In order to facilitate comparison of the results of the several foregoing series of experiments, the following table of the means of each course is subjoined:—

TABLE X.

	Ordinary diet.	Albumen.	Starch.	Gum.
INGESTA.				
Solid.....		8343.20	10357.50	7437.50
Water.....		24598.80	26507.60	29617.50
Total.....		32942.00	36865.10	37055.00
EGESTA.				
<i>Kidneys—</i>				
Whole quantity of urine.....	20898.71	17738.50	18427.67	21538.09
Water.....	19801.13	16019.62	17910.69	21097.50
Solids.....	1097.58	988.87	516.98	440.50
Urea.....	694.63	715.19	215.35	297.13
Uric acid.....	11.67	20.76	7.53	8.81
Chlorine.....	138.13	8.86	16.71	19.21
Sulphuric acid.....	45.18	16.92	9.73	11.12
Phosphoric acid.....	55.85	22.04	13.66	12.28
Residue.....	194.37	215.19	252.86	67.16
<i>Intestines—</i>				
Whole quantity of feces.....	2293.92	3558.36	1107.80	9656.93
Water.....	1673.99	2968.35	886.21	3485.30
Solids.....	619.92	590.02	221.59	6171.62
Ether extract.....	90.60	13.65	36.30	19.96
Alcohol extract.....	95.56	114.58	31.65	15.24
Water extract.....	129.55	102.35	22.69	6074.87
Insoluble residue.....	303.18	358.94	130.95	63.71
<i>Skin and Lungs—</i>				
Total loss by these channels.....		14475.65	17348.54	11917.02
Total egesta.....		35841.42	36879.07	42922.02
Variation in weight*.....		—2899.42	—38.97	—5817.04
Pulse.....	84.23	91.83	87.42	96.49
Temperature of body.....	97.83°	97.39°	98.81°	98.37°
Barometer.....		29.139	29.253	28.915
Thermometer.....		40.41°	6.03°	16.58°

Résumé.

From the preceding investigations, I think the following conclusions (several of which, however, are already well established) fairly deducible, and applicable to the human subject:—

1. That albumen may be assimilated into the system in such quantity as to furnish a sufficiency of both nitrogen and carbon to the organism.

* Owing to neglect to ascertain the weight of the body before commencing the preliminary series of experiments, the mean variation cannot be given.

2. That under the use of an exclusively albuminous diet the nitrogenous constituents of the urine are increased over the ordinary average amounts, though not in proportion to the quantity of albumen absorbed into the circulation.

3. That either some other means than the urine exist for the elimination of nitrogen from the system, or the excess (over two-thirds) is retained in the organism, even when the body is rapidly decreasing in weight.

4. That the continued use of albumen as an article of food increases the proportion of this substance (and of fibrin) in the blood, and in a short time causes it to appear in the urine.

5. That while pure albumen cannot be regarded as of itself adequate to supply the several wants of the system, there is no reason why, when associated with suitable inorganic matters, it should not support both life and health.

6. That starch can be assimilated by the absorbents in more than sufficient quantity to sustain the respiratory function.

7. That under its use the nitrogenous constituents of the urine are very much reduced in amount, even below what would probably occur during inanition, and that, although starch is not capable of nourishing the tissues, it is yet serviceable, aside from its heat-producing power, in retarding their destructive metamorphosis.

8. That the continued use of highly amylaceous food causes the appearance of sugar in the urine.

9. That under the use of such aliments the nitrogenous constituents of the blood are diminished, and the carbonaceous increased.

10. That gum is altogether incapable of assimilation, and therefore possesses no calorific or nutritive power whatever,

but is, on the contrary, a source of irritation to the digestive organs.

11. That in consequence of the above fact, the solids of the urine, during the immediately preceding researches, were entirely derived from the waste of the tissues of the body, and the carbon exhaled by the lungs from the consumption of its fat.

12. That gum, when exclusively used as food, from the irritation it causes in the intestinal canal, and the fact of its non-assimilation, induces more constitutional disturbance than either starch or albumen, and that under a similar condition starch is more productive of ill consequences than albumen.

The investigations which it was the special object of this memoir to detail, are now concluded.

In an essay of this character, whose chief aim is to add to the sum of knowledge, the labors of others could at most receive but a slight notice, and must of necessity frequently be passed over without even a word of recognition. Yet no one appreciates more highly than myself the self-devotion and constant striving to enlarge the bounds of science, which animate so many physiologists of the present day, and which have already yielded such brilliant results. Had I, however, attempted to do justice to even a tithe of their contributions, I should have converted this memoir into a treatise, and might have lost sight of all originality in my efforts to make a successful compilation. With what success I have prosecuted these inquiries is not for me to determine. I cannot, however, think them valueless, for if they only excite others throughout our land to investigate in living beings the operations of nature, they will still be beneficial to the cause of that science which constitutes the basis of all medical knowledge. From the united labors of those who seek by original investigations to build up a positive science, where there is

yet so much darkness and uncertainty, what may we not expect? May we not confidently look forward to the perfect enlightenment of our minds in regard to the most obscure of the vital processes? Though we may often be led astray by experiments conducted without due care, and with insufficient knowledge, they yet afford the only means by which we can successfully work out the sublime problems which the Great Creator of all has proposed for our solution.

ON THE
ALTERATIONS INDUCED BY INTERMITTENT FEVER
IN THE
PHYSICAL AND CHEMICAL QUALITIES OF THE URINE, AND ON
THE ACTION OF THE DISULPHATE OF QUININE.

WE know but little at present concerning the modifications produced by diseases in the function of regressive metamorphosis of tissue, and yet it is very obvious that here our observations, if properly directed, can hardly fail to lead to results of very great importance. The exhalations from the skin and lungs, the urine, and the feces, are so many points upon which to concentrate our efforts; and by carefully studying these several excretions, a vast amount of knowledge may be obtained relative to the pathological actions going on within the system. The facility and exactness with which such inquiries can be prosecuted is only beginning to be perceived, and a rich harvest is reserved for those who will devote themselves to this field of labor.

The condition of the urine in intermittent fever has been observed by Becquerel,* and more recently by Stuart† and others.

* *Séméiotique des Urines*, p 286; and *Traité de Chimie Pathologique*, p. 345.

† *Charleston Medical Journal and Review*, May, 1857, p. 323.

Becquerel's investigations are of the most limited character, being confined to the determination of the specific gravity and general characteristics of the excretion. Stuart's researches are also very unsatisfactory, and not of such a character as to lead to any conclusions worthy of reliance—no means of analysis other than the microscope having been employed.

The action of the disulphate of quinine upon the urine has, within a short period, been investigated by Ranke,* who found that the principal effect of its administration was to diminish the amount of uric acid excreted.

During a recent attack of intermittent fever of the tertian type, I had the opportunity of studying, in my own person, the effects produced by this disease on the physical and chemical qualities of the urine, and also of noticing the results ensuing from the administration of the disulphate of quinine.

There are many obvious advantages to the physiologist, and also to the science which he represents, in basing his conclusions, whenever practicable, on investigations instituted upon himself. He is assured of their correctness, and knows fully the conditions under which they are performed. On the contrary, when others (such at least as are most likely to come under his observation) are the subjects of his researches, he can never be certain that his directions have been complied with, or that he has not been otherwise deceived.

The investigations upon which this paper is based, being confined to one individual, are necessarily not such as to lead to general conclusions, and are only submitted as a slight contribution to our common stock of knowledge. Aside from their correctness, therefore, I have but little to claim for them.

The quantity, specific gravity, and general appearance of the urine were noted, and the amount of its urea, uric acid, free acid,

* Medical Times and Gazette, May 30, 1857, p. 537.

chlorine, and phosphoric and sulphuric acids separately ascertained. The methods used in these determinations were the same as those employed in previous researches, and as elsewhere indicated.

The attack commenced at about $3\frac{1}{2}$ o'clock P.M., on the 4th of January. The cold stage lasted about thirty-five minutes; the hot until near 10 P.M., when profuse perspiration ensued, and I fell asleep, and did not awake till morning.

I was eating a hearty dinner when the paroxysm commenced. At $6\frac{1}{2}$ P.M. I ate a little bread and butter, and drank a cup of tea. At breakfast the following morning I ate as usual. As far as possible, my food was the same throughout the investigations, and my general mode of life was not materially changed.

At the commencement of the cold stage, the bladder was evacuated of its contents. At about $4\frac{1}{2}$ P.M., it was again emptied. The quantity passed at this time amounted to 93·4 cubic centimetres, and had a specific gravity of 1016·35. It was of a pale-straw color, and deposited no sediment on standing. The reaction was feebly acid. Before going to sleep, I passed 283·9 cubic centimetres of urine, having a specific gravity of 1022·19. This was of high color, strong acid reaction, and by morning had deposited a heavy lateritious sediment. On examining this with the microscope, a few crystals of uric acid were perceived.

In the morning, after rising, 495·3 cubic centimetres of urine were evacuated, the specific gravity of which was 1020·43. It was of high color and strong acid reaction. A copious lateritious precipitate was thrown down after a short time; it consisted of urates and a little free uric acid.

For the whole period of twenty-four hours, ending at $3\frac{1}{2}$ P.M. on the 5th, the urine was as follows:—

Quantity.....	1221·7 c. cm.
Specific gravity.....	1020·06
Urea.....	325·18 grains.
Uric acid.....	28·39 “

Free acid.....	39.40 grains.
Chlorine.....	95.42 "
Phosphoric acid.....	69.18 "
Sulphuric acid.....	32.11 "

During the subsequent twenty-four hours of intermission, the urine was of the ensuing character:—

Quantity.....	1650.4 c. cm.
Specific gravity.....	1022.17
Urea.....	480.37 grains.
Uric acid.....	16.84 "
Free acid.....	34.73 "
Chlorine.....	114.58 "
Phosphoric acid.....	52.95 "
Sulphuric acid.....	38.14 "

From these records it is perceived that during the intermission there was an approach to the normal condition of the excretion under consideration. The quantity of urine, its specific gravity, and the amount of urea, chlorine, and sulphuric acid had increased, while at the same time the uric acid, free acid, and phosphoric acid had very considerably diminished.

The second paroxysm came on at about 4 o'clock P.M., on the 6th, and was of similar character to the first. At the termination of the chill, 104.5 cubic centimetres of urine were passed, the specific gravity of which was 1017.41. It was of a pale-yellow color, of feeble acid reaction, and remained clear. During the hot stage I evacuated 325.01 cubic centimetres of urine, of 1021.32 specific gravity, high color, and strong acid reaction. After standing long enough to reduce its temperature sufficiently, a heavy precipitate of urates was thrown down, in which, with the microscope, a few crystals of uric acid were perceived. The urine passed after rising in the morning amounted to 518 cubic centimetres, was of 1022.04 specific gravity, and possessed the characteristics of that last described.

The following table shows the amount and character of the urine for the whole period of twenty-four hours ending at 3½ P.M. on the 7th:—

Quantity.....	1387·2 c. cm.
Specific gravity.....	1019·45
Urea.....	300·16 grains.
Uric acid... ..	31·54 “
Free acid	35·72 “
Chlorine.....	108·11 “
Phosphoric acid.....	72·95 “
Sulphuric acid.....	41·76 “

At 4 o'clock P.M. on this day, I took ten grains of the disulphate of quinia, ten grains at 11 P.M., and the same quantity at 10 A.M. the following day. The paroxysm which would have ensued at about 4 P.M. was thus prevented.

The urine passed during this period of twenty-four hours was of the ordinary normal color, and of tolerably strong acid reaction. No sediment was deposited on standing.

The following table exhibits its characters more in detail:—

Quantity.....	1750 3 c. cm.
Specific gravity.....	1024·67
Urea.....	589·43 grains.
Uric acid.....	13·79 “
Free acid	27·54 “
Chlorine.....	129·83 “
Phosphoric acid.....	55·27 “
Sulphuric acid.....	46·18 “

The presence of quinia was demonstrated by means of Hera-path's test and viewing the crystals formed, with the microscope and by polarized light.

The effects resulting from the administration of the quinine are thus shown to have been well marked. The quantity of urine, its specific gravity, and the amount of urea, chlorine, and

sulphuric acid were increased, while the uric acid, free acid, and phosphoric acid were, on the contrary, diminished.

From 3½ P.M. on this day to the same hour on the following day, I collected the urine evacuated, and submitted it to analysis. No quinine was taken during this period, and no paroxysm of the fever occurred.

Quantity.....	1806·3 c. cm.
Specific gravity.....	1024·81
Urea.....	638·20 grains.
Uric acid.....	12·71 “
Free acid.....	25·80 “
Chlorine	138·27 “
Phosphoric acid.....	56·22 “
Sulphuric acid.....	40·10 “

The above table exhibits pretty nearly the average condition of my urine in its normal state. It is seen that, notwithstanding no quinine was taken, the excretion maintained its general character of the previous day.

No more paroxysms ensued, and circumstances prevented me making at that time any further analysis of the urine.

The accompanying table, in which the several results obtained are collected together, will tend to facilitate reference :—

	1st day. Paroxysm.	2d day. Intermission.	3d day. Paroxysm.	4th day. Administra- tion of quinine	5th day.
Quantity of urine....	1221·7 c. cm.	1659·4 c. cm.	1387·2 c. cm.	1750·3 c. cm.	1806·3 c. cm.
Specific gravity.....	1020·06	1022·17	1019·45	1024·67	1024·81
Urea.....	325·18 grs.	480·37 grs.	300·16 grs.	589·43 grs.	638·20 grs.
Uric acid.....	28·39 “	16·84 “	31·54 “	13·79 “	12·71 “
Free acid.....	39·40 “	34·73 “	35·72 “	27·54 “	25·80 “
Chlorine.....	95·42 “	114·58 “	108·11 “	129·83 “	138·27 “
Phosphoric acid.....	69·18 “	52·95 “	72·95 “	55·27 “	56·22 “
Sulphuric acid.....	32·11 “	35·14 “	41·76 “	46·18 “	40·10 “

From these data it is perceived that, during an attack of intermittent fever, the uric acid and phosphoric acid are very much increased in amount, and the urea and chlorine greatly dimin-

ished. During the intermission there is a close approach to the normal proportions of these constituents, but a subsequent paroxysm restores the former condition. The disulphate of quinia, however, produces a permanent impression on the character of the urine, and, with the return to the natural relations existing between the several substances entering into the composition of this excretion, the disease disappears.

There are several facts indicated by the foregoing researches, to which attention may be directed. Thus the increase in the amount of phosphoric acid eliminated during a paroxysm points strongly to the nervous origin of the disease. The excess in the amount of uric acid excreted, while at the same time the quantity of urea was so strikingly diminished, are facts of the highest importance, and, in connection with the circumstance that during the intermission, and after the administration of the quinine, the urea was increased and the uric acid diminished in quantity, show the close relation existing between these substances, and render more probable the theory that the former body is a product of the continued metamorphosis of the latter.

From so limited an array of facts as the preceding, no hypothesis in regard to the pathology of intermittent fever can be considered as tenable. If, however, the results of these investigations should be confirmed by subsequent observers, a great step will have been made toward a satisfactory theory of this disease, and a rational idea of the therapeutical action of the disulphate of quinine may be formed. The subject is, therefore, left for the present, with the hope that others will turn their attention to the furnishing of material for its elucidation.

The first of these is the fact that the United States is a young nation. It is only about 150 years old, and its history is therefore a history of rapid growth and change. The second is the fact that the United States is a large nation. It covers a vast area of land, and its population is one of the largest in the world. The third is the fact that the United States is a diverse nation. It is made up of many different peoples, each with its own customs and traditions. The fourth is the fact that the United States is a powerful nation. It has a strong economy, a powerful military, and a great influence on the world. The fifth is the fact that the United States is a free nation. It is a land of liberty, where every man is free to follow his own path. The sixth is the fact that the United States is a democratic nation. It is a land where the people have the right to elect their own leaders. The seventh is the fact that the United States is a peaceful nation. It has never been at war with itself, and it has always been a friend to peace. The eighth is the fact that the United States is a nation of progress. It is a land where new ideas are always being tried, and where the future is always being made.

The history of the United States is a story of many things. It is a story of the struggles of the people to create a better life for themselves. It is a story of the triumphs of the people over adversity. It is a story of the growth of the nation from a small colony to a great power. It is a story of the progress of the people towards a more perfect union. It is a story of the peace and freedom that the people have achieved. It is a story of the progress that the people have made. It is a story of the future that the people have created.

ON THE INJECTION OF
UREA AND OTHER SUBSTANCES
INTO THE BLOOD.

THE principal object in view in undertaking the experiments detailed in this paper, was that of deciding upon the correctness of the theory advanced by Frerichs,* explanatory of uræmic intoxication. As is well known, this distinguished author regards the symptoms of blood poisoning, so frequently present in Bright's disease, as not directly depending upon the presence of urea in this fluid, but as being caused by its conversion, through the agency of a ferment, into carbonate of ammonia.

Frerichs performed two series of experiments, which he regards as tending to sustain his hypothesis. In the first series he injected a solution of urea into the blood of animals whose kidneys had been previously removed. In from $1\frac{1}{4}$ to 8 hours they became restless, and vomited. Ammonia was detected in the expired air, and simultaneously convulsions ensued. Death occurred in from $2\frac{1}{2}$ to 10 hours from the commencement of the experiment. Ammonia was found in the blood, the contents of the stomach, and in the bile and other secretions.

In the second series a solution of carbonate of ammonia was

* Die Bright'sche Nierenkrankheit und deren Behandlung.

injected. Convulsions ensued almost immediately, and were quickly followed by stupor. The respiration was labored, and the expired air was loaded with ammonia. This substance, however, gradually disappeared, and the animals recovered their senses.

Frerichs offers no explanation of the nature of the ferment which he conceives to be necessary to produce uræmic poisoning, nor does he even attempt to demonstrate its existence, except indirectly, through the experiments above cited.

While admitting the facts set forth by these experiments, I am constrained to differ with Frerichs in his theory. Ammonia has often been met with as a constituent of the expired air of healthy individuals. I have myself frequently detected it in such cases; it has been demonstrated to be constantly present in the blood; and Frerichs's own experiments (those of the second series) show that it was not capable of causing death even when injected directly into the circulation, and when its presence in the blood was evidenced by its being exhaled in large quantity from the lungs.

The fact that in the first series of investigations the kidneys were extirpated, while in the second the animals were unmutated, while different substances were used in each, prevents our drawing any comparative conclusions from the results obtained.

The experiments to which the present paper relates consisted of two series. In the first the substance was injected into the blood of the sound animal; in the second the kidneys were previously extirpated. The two series were, as far as possible, alike in every other respect. The substances injected in both series were urea, urea and vesical mucus, carbonate of ammonia, nitrate of potash, and sulphate of soda.

FIRST SERIES.

FIRST EXPERIMENT.

UREA.—Into the jugular vein of a large dog I carefully injected 60 grains of urea, dissolved in 4 ounces of distilled water.

No immediate effect was produced. After the lapse of 15 minutes the respiration became more hurried, and the animal began to show signs of uneasiness. At the end of $1\frac{1}{2}$ hours slight spasms of the limbs ensued, and lasted about 10 minutes. These were followed by a disturbed sleep of two hours' duration. The dog then awoke, passed a large quantity of urine, and seemed perfectly well; no other abnormal symptoms occurred.

Ammonia was at no time detected on holding a rod, previously dipped in chlorohydric acid, in the current of the expired air.

The urine of this dog, for the twenty-four hours immediately preceding the commencement of the experiment, amounted to 932 cubic centimetres, and contained 287.39 grains of urea. For the twenty-four hours commencing with the experiment, the quantity of urine was 1268 cubic centimetres, and the urea 341.12 grains—a difference of 336 cubic centimetres of urine and 53.73 grains of urea in favor of the second day. The solid food on both days was the same; the amount of water drank was less on the second day than the first.

From this experiment it is perceived that, of the 60 grains of urea injected into the circulation, 53.73 grains were recovered from the urine, leaving a balance of but 6.27 grains unaccounted for; but which, however, was probably excreted with the urine under some other form.

SECOND EXPERIMENT.

UREA AND VESICAL MUCUS.—60 grains of urea were dissolved in 4 ounces of distilled water, mixed with 115 grains of vesical

mucus,* and carefully introduced into the jugular vein of a dog. The symptoms which followed were almost identical with those of the first experiment, except that the sleep was about 30 minutes longer. On awaking, a large quantity of urine was passed. No ammonia was discovered in the breath. The animal recovered perfectly.

For the twenty-four hours previous to this experiment, the urine of this dog amounted to 823 cubic centimetres, and contained 194.21 grains of urea. For the second period of twenty-four hours the urine amounted to 1459 cubic centimetres, and the urea to 272.86 grains, being an increase of 636 cubic centimetres of urine and 78.65 grains of urea—18.65 grains more than were injected into the circulation. The solid food was the same on both days; the water somewhat more on the second than the first.

THIRD EXPERIMENT.

CARBONATE OF AMMONIA.—60 grains of carbonate of ammonia, dissolved in 4 ounces of water, were injected into the jugular vein of a large dog. Symptoms of great uneasiness almost immediately followed. The animal staggered about the room, and after a few moments fell, and lay panting and moaning on the floor. At the end of two minutes copious fumes of chloride of ammonium were produced by holding a rod, on which were a few drops of chlorohydric acid, to the mouth. Convulsions ensued at the end of $5\frac{1}{2}$ minutes from the commencement of the experiment, and continued 10 minutes. They then ceased, and did not recur. Ammonia continued to be evolved from the lungs for $1\frac{3}{4}$ hours. The dog remained in the recumbent posture for two

* It is well known that to this latter substance is ascribed the power of converting urea into carbonate of ammonia out of the system. I was desirous of ascertaining how far its influence could be exerted in the blood within the system.

hours. Three hours after the commencement of the experiment he evacuated a quantity of ammoniacal urine. He recovered perfectly.

During the twenty-four hours preceding this experiment, the dog eliminated 1327 cubic centimetres of urine, which contained 345.82 grains of urea. For the succeeding period the quantity of urine was 1654 cubic centimetres, and the amount of urea 296.53 grains, an increase of 227 cubic centimetres in the urine, and a diminution of 48.29 grains in the urea. The food was of the same character and quantity on both days; the amount of water drank was slightly greater on the second day.

The symptoms observed after the introduction of the carbonate of ammonia into the blood, it is seen, did not correspond altogether with those which followed in Frerichs's investigations. Thus, there was no vomiting nor stupor, and the convulsions were not of so violent a character. The quantity of carbonate of ammonia injected by Frerichs is not stated by him, and the difference in the effects may be due to a difference in the amount of this substance introduced into the circulation.

FOURTH EXPERIMENT.

NITRATE OF POTASH.—I injected 60 grains of nitrate of potash, dissolved in 4 ounces of water, into the circulation of a medium-sized dog. Convulsions of a violent character almost instantly ensued, and continued, with occasional intermissions, for $1\frac{3}{4}$ hours. There was also vomiting and severe retching. Stupor followed, and lasted till the death of the animal, which took place at the end of 5 hours and 25 minutes from the commencement of the experiment. No ammonia was detected in the breath.

FIFTH EXPERIMENT.

SULPHATE OF SODA.—60 grains of sulphate of soda, dissolved in 4 ounces of water, were injected into the jugular vein

of a medium-sized dog. Convulsions quickly followed, and were very severe, lasting about two and a half hours, with short intermissions. The dog vomited twice. Stupor ensued upon the convulsions, and was present for about three hours. The dog gradually recovered his senses, but was disposed to remain quiet for the balance of the day. The next day he seemed entirely well.

The urine of the twenty-four hours preceding the experiment amounted to 1125 cubic centimetres, and the urea to 211·34 grains. For the twenty-four hours commencing with the experiment, the quantity of urine was 1283 cubic centimetres, and of urea 201·15 grains—an increase in the urine of 158 cubic centimetres, and a decrease in the urea of 6·19 grains.

SECOND SERIES.

In this series, as before remarked, the kidneys were removed previously to the introduction of the substances experimented with into the circulation. Extirpation of these organs is not necessarily attended with an immediately fatal result. A dog will live from one to four days after this operation, when it has been carefully performed.

FIRST EXPERIMENT.

UREA.—I removed the kidneys from the dog used in the first experiment of the foregoing series. He bore the operation exceedingly well, and even appeared somewhat lively after it. Three hours subsequently I injected 60 grains of urea, dissolved in 4 ounces of water, into the jugular vein. Convulsions ensued at the end of 45 minutes, and continued with alternations of stupor for $6\frac{1}{4}$ hours, when the animal died. There was no vomiting. No ammonia was at any time detected in the breath.

The post-mortem examination showed a healthy condition of the stomach and bowels. No ammoniacal odor was perceived.

A portion of the fluid contents of the stomach were mixed with a little caustic baryta, in a test tube, and gently heated. On holding a glass rod, moistened with chlorohydric acid, over the mouth of the tube, no fumes of chloride of ammonium were formed, showing, therefore, the absence of ammonia.

By employing caustic potash instead of baryta, and then applying the glass rod as before, copious fumes of the chloride of ammonium were produced. This arose from the conversion of the urea present into carbonate of ammonia through the action of the potash.

The presence of urea in the stomach was directly determined by evaporating a portion of the fluid contents to dryness, at a low heat, by means of the water bath, treating the residue with alcohol, and again evaporating to dryness. By digesting the solid residue with warm water, filtering, and adding nitric acid to the filtrate, crystals of nitrate of urea were formed in considerable quantity.

The fact that no ammonia was discovered in the breath or contents of the stomach of this animal is in direct opposition to the results of Frerichs's experiments. I think it will be generally admitted that had any ammonia been present it would have been detected by the means employed, and, conjoined to the fact that so unequivocal evidences of the existence of urea in the stomach were indicated, leave no doubt of the non-conversion, in this instance at least, of the urea into carbonate of ammonia.

The death in this case is, therefore, I think, fairly to be attributed to the direct action of the urea upon an organism brought into an abnormal condition by removal of the kidneys. In Bright's disease a similar condition of the system is present, and may exercise a like influence over the action of the urea which has accumulated in the blood.

SECOND EXPERIMENT.

UREA AND VESICAL MUCUS.—Having previously extirpated the kidneys from the dog used in the corresponding experiment of the foregoing series, I injected into the circulation 60 grains of urea, dissolved in 4 ounces of water, to which 115 grains of vesical mucus had been added. The dog remained quiet for nearly an hour, when violent convulsions ensued, and continued with but slight intermissions for $5\frac{1}{2}$ hours. Vomiting of bilious matters occurred twice. Stupor followed the convulsions, and remained till death, which took place at the end of 8 hours and 20 minutes from the commencement of the experiment.

No ammonia was detected in the expired air or vomited matters, nor was any discovered after death in the contents of the stomach. Urea was indicated in these latter by the method employed in the previous experiment.

The same remarks are applicable to this experiment as to the preceding, as the results are almost identical. In addition, it will be remarked that the mucus injected exercised no influence on the composition of the urea introduced into the circulation with it.

THIRD EXPERIMENT.

CARBONATE OF AMMONIA.—After extirpating the kidneys, I injected into the jugular vein of the dog previously used in the corresponding experiment of the preceding series, 60 grains of carbonate of ammonia, dissolved in 4 ounces of water. Convulsions ensued in five minutes, and continued almost uninterruptedly for $3\frac{1}{2}$ hours. Stupor followed, and remained present till the death of the animal, which took place 6 hours and 18 minutes from the commencement of the experiment. During the convulsions there was several times vomiting of chyme and mucus which gave off a strong ammoniacal odor.

Ammonia was detected in the breath in $2\frac{1}{2}$ minutes after the injection into the blood. No post-mortem examination was made.

From this experiment it is seen that carbonate of ammonia is speedily fatal after being introduced into the circulation of an animal deprived of its kidneys.

FOURTH EXPERIMENT.

NITRATE OF POTASH.—60 grains of nitrate of potash were introduced, dissolved in 4 ounces of water, into the circulation of a medium-sized dog whose kidneys had been removed three hours before. Convulsions followed in $4\frac{1}{2}$ minutes, and continued for $3\frac{1}{2}$ hours, when the animal died. There was neither vomiting nor stupor, but undoubted evidence of the existence of ammonia in the breath was obtained. The post-mortem examination showed a congested condition of the lungs and of the vessels of the stomach.

FIFTH EXPERIMENT.

SULPHATE OF SODA.—I removed the kidneys from the dog used before in the corresponding experiment, and 3 hours afterward injected 60 grains of sulphate of soda, dissolved in 4 ounces of water, into his circulation. Convulsions came on in 3 hours and 20 minutes, and lasted about 2 hours, when stupor supervened, and the animal quickly died. There was no vomiting. No post-mortem examination was made.

Judging from the foregoing experiments, I think that Frerichs's theory of uræmic intoxication is erroneous. In neither of the cases in which urea was injected into the circulation was any ammonia detected in the breath, vomited matters, or contents of the stomachs of the animals. Without pretending to question

the accuracy of Frerichs's statement relative to the discovery of ammonia in his experiments where urea was injected, I am of the opinion that its presence was accidental, and that it is not to be regarded as an invariable attendant upon the retention of urea in the system.

Removal of the kidneys would seem to exercise a very important influence over the action of substances which, when introduced directly into the blood of sound animals, are not capable of causing death, or even of producing much constitutional disturbance. Thus, of ten animals experimented upon in the first series, but one (that in which nitrate of potash was injected) died, while all of the second series were attacked with convulsions, and sank after a few hours. It is seen, therefore, that carbonate of ammonia is not more poisonous than the other substances used, and not so much so as nitrate of potash.

The condition of system remaining after extirpation of the kidneys is, in many respects, analogous to that present during Bright's disease. In the latter condition the kidneys act imperfectly, and many substances which should be eliminated are retained in the organism. In the former there is of course no excretion of matter through these channels. In all cases, so far as I am aware, where the kidneys of animals have been extirpated and urea injected into the blood, death has supervened in a much shorter time than would have been the case had no urea been thus introduced into the system. I see, therefore, no great difficulty in ascribing the condition known as uræmic intoxication to the direct action of an excessive accumulation of urea in the system.

The fact that urea in large quantity has been found in the blood of persons suffering under Bright's disease, but in whom no symptoms of blood poisoning were present, is no argument against the correctness of this view, for, doubtless, as with most other poisons, all persons are not alike sensitive to its action.

Moreover, when the disease progresses slowly the rate of accumulation of urea is also slow, and thus the system, by becoming in a manner habituated to its presence, may be enabled to endure an excess without symptoms of intoxication necessarily attending.

I conclude, therefore, from the foregoing experiments—

1st. That urea, (simple and combined with vesical mucus,) carbonate of ammonia, and sulphate of potash, when injected into the blood-vessels of sound animals, do not cause death.

2d. That nitrate of potash, when thus introduced, is speedily fatal.

3d. That death ensues from the injection of any of the foregoing named substances into the circulation of animals whose kidneys have been previously extirpated.

4th. That in neither case does urea, when introduced directly into the circulation, undergo conversion into carbonate of ammonia.

ON THE ACTION OF CERTAIN VEGETABLE DIURETICS.

THE ensuing investigations consist mainly of repetitions of those performed some years since by Krahmer, and subsequently by Bird. They have reference to the appreciation of the influence of squill, juniper, digitalis and colchicum, over the quantity of the urine, its specific gravity, and the amount of its solid organic and inorganic constituents. They were all performed upon healthy adult males.

The quantity of urine was determined in cubic centimetres, and the weight of the solids in grammes.

The method employed for the determination of the whole amount of solid matter was as follows:—

Ten cubic centimetres of the urine were evaporated to as complete dryness as possible *in vacuo* over sulphuric acid, and the residue accurately weighed. By simple proportion, the amount of solids in the whole quantity of urine was easily ascertained.

Although it is impossible to get rid of all the water by this process, the quantity remaining is extremely small, and the results obtained are far more accurate than those yielded by evaporating to dryness in the water bath as generally practiced. No matter how carefully this latter method is conducted, the loss of urea by decomposition is always an important item, and involves far more serious errors than the imperfect desiccation by the former process.

For the determination of the amounts of organic and inorganic constituents separately, the solid residue obtained as above was mixed with ten or fifteen drops of moderately strong nitric acid, and gently heated till the mass was well dried. The heat was then gradually raised till all the carbon was consumed, and the mass in consequence became white. It was then cooled *in vacuo* over sulphuric acid and weighed. The inorganic matter was thus determined, and the loss showed the proportion of organic substance.

Digitalis.—The subject of the experiments with this substance was about twenty-five years of age, and in good health. For the three days immediately preceding the commencement of the investigations, the average quantity of urine daily excreted by him was 1474·5 cubic centimetres, the specific gravity was 1024·30, and the average total amount of solid matter was 75·31 grammes, of which 30·17 grammes were inorganic and 45·14 organic constituents. The digitalis was given in the form of the official tincture in doses of 20 minims, three times in twenty-four hours, and was continued for three consecutive days. During this period the manner of living (food, drink, exercise, etc.) was as nearly as possible the same as during the preliminary investigations.

First day.—The urine passed on this day was of a pale-straw color and feeble acid reaction; quantity, 1950 cubic centimetres; specific gravity, 1013·25; total solids, 69·98 grammes, of which amount 31·27 were inorganic and 38·71 organic matter. The action of the digitalis was not manifested otherwise than by its effect upon the urine.

Second day.—The urine passed on this day was of similar physical character to that above mentioned. The quantity was 1873·6 centimetres, the specific gravity 1014·32, and the total solids 63·74 grammes. The inorganic solids amounted to 30·15 grammes, and the organic to 33·49.

The pulse on this day was somewhat slower and fuller than on the previous day.

Third day.—The quantity of urine evacuated on this day was 1624·9 cubic centimetres, and of specific gravity 1020·04. The total amount of solid matter was 67·29 grammes, of which 33·19 were inorganic and 34·10 organic.

The color, reaction, and odor of the urine were similar to those of the two previous days.

The characteristic effects of the digitalis upon the action of the heart were well marked during this day.

The effect of the digitalis in increasing the amount of urine is seen to have been greatest on the first day. On the second day it had fallen somewhat, and on the third was but 150 cubic centimetres greater than when no digitalis was taken. The solids, it is seen, were less than the normal standard from the commencement, were still further reduced on the second day, and on the third were slightly increased. This diminution is perceived to have been owing to the lessened amount of organic matter excreted. The inorganic substances were somewhat increased in amount over the ordinary proportion.

Juniper.—The experiments with this substance were conducted on a healthy man thirty-five years of age. The average condition of his urine for the three days immediately preceding the investigations was as follows: Quantity, 1237·5 cubic centimetres; specific gravity, 1022·50; total solids, 61·23 grammes, of which 23·12 were inorganic and 38·11 organic matter. It was of ordinary color and odor, and of strong acid reaction.

Sixteen ounces of the officinal infusion of the berries of the *Juniperus communis* were taken during the twenty-four hours, and the manner of living kept as nearly as possible to correspond with that of the preliminary experiments.

First day.—For this day the quantity of urine amounted to 1732 cubic centimetres, the specific gravity of which was 1016·38; the total solids were 62·75 grammes; of this amount, 25·43 grammes were inorganic and 37·32 organic constituents.

The urine was of a pale-straw color, and gave off the characteristic odor produced by juniper. The reaction was feebly acid.

Second day.—The quantity of urine passed on this day was 1885·2 cubic centimetres. The specific gravity was 1014·15, and the total solids 58·49 grammes, 22·17 of which were inorganic and 36·22 organic matter. The physical characteristics were similar to those of the day before. The reaction was barely acid.

Third day.—On this day the quantity of urine was 1672·5 cubic centimetres, with a specific gravity of 1018·41. The total solids amounted to 63·27 grammes, of which 27·50 were inorganic and 35·73 organic matter. The physical characteristics and reaction were the same as on the previous day.

From these experiments it is seen that while the quantity of urine was materially increased by the juniper, the amount of solid matter, as a whole, was but slightly affected, the loss in organic matter being about compensated for by the increase in the inorganic.

Squill.—The experiments with this substance were instituted upon myself, and were conducted upon the same general principles as the foregoing series. The average daily quantity of urine, for the three days preceding the investigations, was 1358 cubic centimetres. The specific gravity was 1023·51, and the total solids 69·35 grammes; of this amount 27·22 were inorganic and 42·13 organic matter.

I took two grains of the dried bulb of the *Scilla maritima* three times in the twenty-four hours; the other conditions remaining the same as in the preliminary examination of the urine.

First day.—The quantity of urine passed on this day was 1572 cubic centimetres of 1020·34 specific gravity. The total solid matter was 60·67 grammes, 31·07 of this amount being inorganic and 29·60 organic constituents. The urine was of feeble acid reaction.

Second day.—Quantity of urine, 1493·5 cubic centimetres; specific gravity, 1020·90; total solids, 58·22 grammes; inorganic matter, 30·15; organic, 28·07 grammes. The reaction, etc. were the same as on the preceding day.

Third day.—On this day the quantity of urine amounted to 1535 cubic centimetres, and was of 1019·37 specific gravity. The total amount of solid matter was 61·58 grammes, of which 30·58 were inorganic and 31·00 organic constituents. The reaction, color, etc. were unchanged.

From the above experiments it is perceived that the action of the squill was similar to that of the digitalis and juniper, *i.e.* causing an increase in the water of the urine and inorganic solids, but a reduction of the amount of organic matter. The loss of organic matter was considerably greater than with either of the other substances.

Colchicum.—The investigations into the action of this substance were performed upon a healthy man, twenty-eight years of age. The urine, for the three days immediately preceding the commencement of the experiments, was of the following daily average character: Quantity, 1230 cubic centimetres; specific gravity, 1025·08; total solids, 63·12 grammes; inorganic matter, 29·83, and organic, 33·29. The reaction was very strongly acid.

One and a half drachms of the officinal tincture of the seeds of the *Colchicum autumnale* were given three times in twenty-four hours, and continued for three days. During this period the food, exercise, etc. were as nearly as possible the same as during the preliminary series.

First day.—The quantity of urine passed on this day was 1595·7 cubic centimetres, with a specific gravity of 1024·37. The total solids amounted to 77·29 grammes, the inorganic matter of which was 36·50 grammes and the organic 20·79 grammes. The reaction was strongly acid.

Second day.—Quantity of urine, 1484·1 cubic centimetres;

specific gravity, 1024·31; total solids, 75·22 grammes. The amount of inorganic matter was 35·01 grammes, and of organic, 40·21. The reaction was very strongly acid.

Third day.—On this day the quantity of urine amounted to 1620 cubic centimetres, and was of 1022·06 specific gravity. The total amount of solid matter was 79·33 grammes, of which 34·20 were inorganic and 45·13 organic constituents. Reaction strongly acid.

It is thus perceived that the action of the colchicum, as compared with that of the other substances experimented with, was very remarkable, it being the only one with which there was an increase in the amount of solid matter eliminated, both organic and inorganic.

From the foregoing experiments, the following table, embracing the averages of each series of investigations, is constructed:—

	Quantity of urine.	Specific gravity.	Total solids.	Inorganic solids.	Organic solids.
Normal standard.....	1474·5	1024·30	75·31	30·17	45·14
Digitalis.....	1822·8	1015·87	67·00	31·54	35·43
Normal standard.....	1237·5	1022·50	61·23	23·12	38·11
Juniper.....	1763·2	1016·28	61·50	25·03	36·42
Normal standard.....	1358	1023·51	69·35	27·22	42·13
Squill.....	1533·5	1020·20	60·15	30·00	29·55
Normal standard.....	1280	1025·08	63·12	29·83	33·29
Colchicum.....	1550·6	1023·58	77·28	35·23	42·04

From the foregoing investigations, I think it is deducible that neither digitalis, juniper, nor squill increases the total amount of solid matter eliminated by the kidneys, and that the organic matter is considerably reduced through their influence. Although they do increase the amount of inorganic matter removed through the urine, yet as it is the organic matter which is generally con-

sidered as contaminating the blood in disease, it is evident they exert no effect whatever in deprating this fluid, but, on the contrary, are positively injurious.

The results obtained, in so far as the experiments with digitalis, squill, or juniper are concerned, are similar to those obtained by Krahmer, but are materially different as regards the colchicum. For, although Krahmer found that under the influence of this medicine there was an increase in the amount of organic matter excreted, this was so small as to lead to the supposition that it may have been accidental, and besides there was a reduction in the quantity of inorganic substance removed. It is desirable, therefore, that we should have further observations with this article.

EXPERIMENTAL RESEARCHES

RELATIVE TO

CORROVAL AND VAO:

TWO NEW VARIETIES OF WOORARA, THE SOUTH
AMERICAN ARROW-POISON.*

THE history of the remarkable poison which we design to consider in the present memoir has been so well detailed by M. Cl. Bernard,† that it would be useless for us to enter fully into this portion of the subject. We shall, accordingly, confine ourselves more particularly to an examination of those accounts which relate to the discovery and mode of preparation of the substance in question, and to the indication of a few statements which have escaped M. Bernard's attention.

Woorara was first introduced to the civilized world in 1595, by Sir Walter Raleigh,‡ on his return from Guiana. The following quotation describes graphically, but with much exaggeration, the action of the poison :—

“There was nothing whereof I was more curious, than to finde

* This paper is the result of the joint labors of Dr. S. Weir Mitchell, of Philadelphia, and myself. He is more immediately responsible for the part relating to vao, and I for the remainder. In all the experiments of my part I had the constant benefit of his advice and assistance.

† *Leçons sur les Effets des Substances Toxiques*, etc., 1857, p. 238.

‡ Raleigh's *Discoverie of Guiana*. Printed for the Hakluyt Society. London, 1848.

out the true remedies of these poisonous arrowes; for besides the mortalitie of the wound they make, the partie shot indureth the most insufferable torment in the world, and abideth a most uglye and lamentable death, sometimes dying starke mad, sometimes their bowels breaking out of their bellies, and are presently discoloured as blaek as pitch, and so unsavoury as no man can endure to cure or attend them, and it is more strange to know that in all this time there was never Spaniard, either by gift or torment, that could attaine to the true knowledge of the cure, although they have martyred and put to invented torture I know not how many of them. But every one of these Indians know it not, no, not one among thousands, but their soothsaiers and priests who do conceale it and only teache it but from the father to the sonne."

Garcilasso de la Vega* states that the Indians of Peru poisoned their arrows with a species of herb, and that symptoms of poisoning were not produced till about three days after the wound was given; death followed in seven days afterward, the sufferer raving, eating or gnawing his own flesh, and beating his brains against the wall.

Another kind of poison is spoken of by De la Vega, in which the decomposing matters of human flesh form an important constituent. Previous to the arrival of the Spaniards, the flesh of the natives was employed for this purpose; but conceiving the idea that the flesh of a red-headed Spaniard possessed more heat and virulency than that of their own people, they subsequently employed this material whenever it fell in their way.

De la Condamine† states that the poison used by the Indians of South America is extracted by means of heat from the juice of

* History of Peru, chap. xxxvii. p. 741.

† Relation abrégé d'un Voyage fait dans l'Intérieur de l'Amérique Méridionale, etc. Mémoires de l'Académie des Sciences, tome xii. 1745, p. 391.

several plants, and especially from certain *lianes*, [in Spanish, bejucos, in English, bind-weeds.] He asserts that there are over thirty kinds of plants in the Ticunas poison.

Bancroft* is more explicit, and gives the following formula for the woorara:—

“Bark of the root of the wooraro, six parts;

“Bark of the warracobba corra, two parts;

“Barks of the root of coranapi baketi, and of hatchybaly, of each one part.

“All these are to be finally scraped and put into an Indian pot and covered with water. The pot is then to be placed over a slow fire that the water may simmer for a quarter of an hour. After which the fluid is to be expressed from the bark by the hands, taking care that the skin is unbroken; this being done, the bark is to be thrown away and the juice evaporated over a moderate fire to the consistence of tar, when it is to be removed.

“The smallest quantity of this poison conveyed by a wound into the red blood-vessels of an animal, causes it to expire in less than a minute, without much apparent pain or uncasiness, though slight convulsions are sometimes seen near the instant of expiration.”

According to Fermin,† the Indians of Surinam poison their arrows by dipping them to the height of two inches in the juice of a tree called *mancelinier*.

“As soon as an incision is made in this tree, a milky and acrid substance flows out, filled with particles so volatile that the poison is as prompt as violent. It remains active for a long time after the arrows are dipped into it, as I have myself proved in several instances, by shooting animals with arrows which had been poisoned four or five years previously. Death ensued in

* Essay on the Natural History of Guiana. London, 1769, p. 288.

† Description Générale Historique, Géographique et Physique de la Colonie de Surinam. Amsterdam, 1769, p. 52.

half an hour after the wounds were inflicted. I have these arrows still in my possession, and have no doubt that the poison is as active as ever. To show how pernicious it is when recent, the following experiment is adduced :—

“In order to convince the Spaniards, an Indian king wounded a child, twelve years of age, slightly in one of the toes, with a poisoned arrow, and immediately ordered the surgeons whom he had summoned to amputate the limb. This was scarcely done when the Spaniards saw the child expire, not in consequence of the operation, as was fully verified, but from the effects of the poison which was suddenly thrown into the mass of the blood, and had rapidly reached the most important organs, before relief could be afforded.”

Humboldt* gives a full account of the woorara, and denies many of the absurd statements of previous writers. He was present during the manufacture of the poison at Esmeralda, and states that it is derived from the bark and alburnum of the *bejuco de mavacoure*, a species of bind-weed, belonging to the strychnos family. The fresh juice of this plant is not regarded as poisonous, probably, as Humboldt states, on account of its not being in a concentrated condition. The manner of preparing the poison is as follows :—

“A cold infusion is first prepared by pouring water on the fibrous matter, which is the ground bark of the *mavacoure*. A yellowish water filters during several hours, drop by drop, through the leafy funnel. This filtered water is the venomous liquor, but it acquires strength only when it is concentrated by evaporation, like molasses, in a large earthen pot. The Indian, from time to time, invited us to taste the liquid; its taste, more or less bitter, decides when the concentration by fire has been carried suffi-

* Personal Narrative of Travels to the Equatorial Regions of the New Continent during the years 1799-1804. 2d edition. London, 1827, vol. v. p. 519.

ciently far. There is no danger in this operation, the *curare* being deleterious only when it comes into immediate contact with the blood. The vapors, therefore, which are disengaged from the pans are not hurtful, notwithstanding what has been asserted on this point by the missionaries of the Orinoco."

In order to give body to the extract, another vegetable juice of a very glutinous character is added. The mass thus formed constitutes the *curare* of commerce.

Another species of the poison prepared entirely from the root is less active.

According to Waterton,* the *woorara* is prepared by the Macousi Indians in the following manner:—

The materials required are the *woorali* vine, a bitter root, one or two bulbous plants, two species of poisonous ants, some strong Indian pepper, and the fangs of the *labarri* and *corra-couchi* snakes. Having procured these materials, the Macousi proceeds as follows:—

"He scrapes the *woorali* vine and bitter root into thin shavings, and puts them into a kind of colander made of leaves; this he holds over an earthen pot and pours water on the shavings; the liquor which comes through has the appearance of coffee. When a sufficient quantity has been procured, the shavings are thrown aside. He then bruises the bulbous stalks and squeezes a proportionate quantity of their juice through his hands into the pot. Lastly, the snakes' fangs, ants, and pepper are bruised and thrown into it. It is then placed on a slow fire, and as it boils, more of the juice of the *woorali* is added according as it may be found necessary, and the scum is taken off with a leaf; it remains on the fire till it is reduced to a thick syrup of a dark-brown color. As soon as it has arrived at this state, a few arrows are poisoned with it to try its strength."

* Wanderings in South America, p. 51.

Schomburgk* asserts with much confidence that the woorara is prepared entirely from vegetable substances, the chief of which is the bark of the *strychnos toxifera*. According to this author, the following experiment was instituted by his brother: A gallon of water was added to two pounds of the bark of the *strychnos toxifera*, and allowed to remain for twenty-four hours. Half of the fluid, which was already of a brown color, was then put into another vessel and evaporated over a slow fire to a syrupy consistence, the remaining half of the fluid being added as evaporation progressed. Two chickens were then wounded with instruments charged with the extract, one in the foot, the other in the neck. Symptoms of poisoning were evident in five minutes. The first died in twenty-seven minutes, the other in twenty-eight minutes after the infliction of the wounds. It is thus shown that the extract of the bark of the *strychnos toxifera* alone, when introduced into the circulation, is speedily fatal.

Schomburgk, moreover, had an opportunity, as he states, of witnessing the preparation of the woorara by an Indian. According to the account which he gives, three species of the *strychnos* enter into its composition, besides six other plants. No animal matter of any kind was used in its manufacture.

According to Osculati,† the poison prepared by the Indians of the province of Esmeralda, and which is called *ciguela*, is extracted from a tree, and is not to be compared in virulence with the ticunas. The *ciguela* will kill a small animal in about ten minutes, but is not fatal when introduced into the human system, causing only pustules and malignant ulcerations. He also refers to another arrow-poison prepared by the Colorados.

Osculati‡ also states that the Orckones and Ticunas are ele-

* Reisen in Britisch Guiana. Leipzig, 1847. Band i. s. 445 et seq.

† Esplorazione delle Regione Equatoriale. Milano, 1850, p. 108.

‡ Op. cit., p. 207.

brated for the manufacture of certain active poisons which kill in two or three minutes. These poisons vary very much in composition among the several tribes. The *ticunas*, or *huarare*, mixed with the *lamas*, a poison prepared by the Lamas Indians, forms a toxic compound fatal to all animals. The *ticunas* alone is not fatal to quadrupeds or birds. The *lamas* is considered to be more active, but even this is not fatal to quadrupeds. In a note it is stated that having sent a few small fragments of the poison to Prof. Luigi Patellini, experiments were instituted with it by this gentleman. A guinea-pig, poisoned with it, died in about five minutes in tetanic convulsions. The temperature of the body fell at once.

Dalton* repeats Waterton's account of the method of manufacturing the *woorara*, and adds little if any additional information on the subject. He also states, after Hartsinck, that the Indians test the virulence of the poison by shooting arrows charged with it into trees. If the leaves drop off or wither within three days it is deemed sufficiently powerful.

It is highly probable, as Tschudi† asserts, that the poison used for weapons by the South American Indians varies with every tribe. This traveler declares that, notwithstanding all assertions to the contrary, animal poisons do enter into the composition of the arrow-poison used by the Indians of Peru. His evidence, however, is only of a hearsay character, as he never witnessed the preparation.

Hernndon‡ who, however, does not seem to have paid particular attention to this point, but whose evidence, as far as it goes, is in every way reliable, asserts that the arrow-poison used by the Indians of the Amazon is of a vegetable character, and prepared

* History of British Guiana. London, 1855, vol. i. p. 68.

† Travels in Peru. English edition. London, 1847, p. 407.

‡ Exploration of the Valley of the Amazon, by Lieut. W. Lewis Hernndon, U. S. Navy. Washington, 1853. p. 140.

from the juice of a creeper called *bejuco de ambihuasca* mixed with *aji* or strong red pepper, *barbasco*, *sarnango*, and any other poisonous substances known to the Indians.

Taking the accounts of the several authors we have quoted, as well as the evidence of others who have written on the subject, into consideration, we cannot avoid coming to the conclusion that a great deal of uncertainty still exists relative to the substances and method used in the preparation of the woorara. The earlier accounts on this point are so distorted with manifestly erroneous ideas, and so exaggerated in their detail, that we can place but little reliance upon them. Among later writers, Schomburgk is, perhaps, more to be depended upon than any other, both on account of general accuracy and high scientific attainments; but it is almost certain that every tribe has its own distinct poison, differing more or less from that of every other tribe. The evidences we have to submit on this point, from our own researches, will, we think, abundantly establish the fact of the different physiological effects resulting from poisoning in the different specimens of woorara, and consequently clearly indicate a difference in composition.

Physical and Chemical Properties.—The woorara obtained by Baneroff* is stated by him to have possessed the following properties: It was liquefiable by heat, and dissolvable in water, alcohol, hydrochloric acid, and liquor ammoniæ, as also in blood, saliva, etc., except a very small part which subsided both in a spirituous and aqueous menstruum, and consisting, as he thinks, of earthy particles foreign to the composition. It united with acids without emotion or change of color. On mixing it with alkalies, no ebullition was perceptible, but the color changed from a reddish-brown to a yellowish-brown. A few grains, mixed with as many ounces of human blood, entirely prevented a separa-

* Op. cit., p. 291.

tion of serum and crassamentum, and the whole mass continued in a state of fluidity.

The first reliable and thorough examination made of the woorara, and one which even yet has not been excelled in completeness, was that of MM. Roulin and Boussingault.* The specimen examined by these chemists was obtained from the Rio Negro. It was a solid extract, black, of a resinous appearance, of a brown color when reduced to powder, and of an intensely bitter taste. This bitterness was unaccompanied by acidity or sharpness. It burned with difficulty, and in consuming gave off no odor of organic nitrogenous substances.

It was but slightly soluble in sulphuric ether, more so in alcohol, forming a beautiful red and very bitter tincture. In water it was soluble to a considerable extent, forming an intensely bitter infusion, of slight acid reaction to litmus paper.

By further investigation, MM. Roulin and Boussingault arrived at the conclusion that no strychnia was present. They, however, obtained an alkaline principle soluble in water, for which the name of *curarin* has been proposed. This substance they obtained by the following procedure:—

The woorara was reduced to powder, and treated repeatedly with boiling alcohol. The alcoholic extract was evaporated, and the residue treated with water, which dissolved the active principle, leaving nothing but a little resinous matter. The aqueous solution was then decolorized by animal charcoal, and treated with infusion of galls. A beautiful whitish-yellow flaky precipitate was thrown down.

The precipitate thus obtained was well washed, heated to ebullition in water, and dissolved by the addition of oxalic acid. The acid liquor was then supersaturated by magnesia and fil-

* Examen Chimique du Curare, Poison des Indiens de l'Orinoque. Annales de Chimie et de Physique, tome xxxix. 1828, p. 24.

tered. It was again evaporated to dryness, and the residue dissolved in alcohol. This solution was concentrated and spontaneously evaporated to a syrupy consistence. It was then further concentrated by evaporation *in vacuo*.

Thus obtained, the *curarin* was a solid transparent mass, of an excessively bitter taste, and possessed in an eminent degree of all the virulence of the woorara. It was not crystallizable, was of a pale-yellow color, and strongly attractive of moisture from the atmosphere. It formed salts with sulphuric, nitric, hydrochloric, and acetic acids, none of which were crystallizable.

MM. Roulin and Boussingault are of the opinion that the normal acid of the woorara is the acetic.

The results of the examination made by the above named chemists were subsequently confirmed by MM. Pelletier and Petroz.*

Heintz† has also examined the woorara chemically. By adding tannic acid to the aqueous solution of this substance, he obtained an abundant precipitate soluble in boiling water. This was taken from the filter, boiled with magnesia, and then evaporated to dryness. The extract thus obtained was then treated with alcohol, to remove it from any insoluble salts of magnesia, and the solution again evaporated to dryness. By this means a yellowish-brown extract was obtained, possessing no alkaline reaction, but endowed in an eminent degree with the toxic principle of the woorara. Heintz does not regard this extract as at all pure. He afterward employed both the bichlorides of mercury and platinum to effect the precipitation, but with no better success, a yellowish-brown extract being still obtained.

By Lassaigne's method Heintz convinced himself that the ex-

* Examen Chimique de Curare. Annales de Chimie et de Physique, tome xl., 1829, p. 213.

† Reisen in Britisch Guiana. Von Richard Schomburgk. Band i. s. 452, (note.)

tract contained nitrogen. He also found sugar, gum, resin, extractive matter, tannic and gallic acids, and traces of saline combinations with organic acids—probably the tartaric and oxalic.

He was unable to find the least trace of strychnia.

Dr. Brainard,* of Chicago, asserts that by an analysis, undertaken at his suggestion, formic acid and a proteinaceous substance were detected in the woorara. None of the details of the analysis are given, and we must therefore await further particulars before accepting such a statement.

Dr. Brainard,† in conjunction with Dr. Green, of New York, presented a communication to the French Academy of Sciences, in which the opinion is expressed that the poisonous action of the woorara is probably due to the venom of certain reptiles. Boussingault,‡ however, in the debate which followed, denied the existence of any animal matter in the woorara; and in a subsequent paper, in which the whole subject of woorara is well discussed, Dr. Green§ doubts the existence of animal poison in the substance in question.

From our own investigations, as well as from those we have referred to, we think it highly improbable that the activity of the woorara is due to animal matters. Doubtless it is true that some Indians introduce the fangs, livers, etc., of venomous reptiles into their arrow-poison, but it is scarcely possible that such substances, even if poisonous in the first instance, would retain their activity through the process of manufacture which the woorara undergoes. When we come to detail our own observations, we

* Smithsonian Report, 1854, p. 123 et seq.

† Comptes Rendus, tome xxxviii., 1854, p. 411 et seq.

‡ Op. cit., p. 414.

§ American Medical Gazette, vol. vii. No. 1, (new series,) Jan., 1858, p. 2 et seq. See also vol. vi. No. 5, May, 1855, and vol. vi. No. 7, July, 1855, for Dr. Green's other important papers on this subject.

shall return to this point, so far as it relates to the varieties of this poison with which we have experimented.

Physiology.—The earliest recorded experiments with woorara, of a systematic character, to which we have been able to refer, are those of De la Condamine,* who relates that his observations were made with arrows which he had possessed for more than a year.

In presence of several high personages a chicken was slightly wounded with a small arrow charged with the poison. It died in seven minutes and a half. Another, pricked in the wing with a similar arrow, died very soon in convulsions, notwithstanding sugar, an alleged antidote, was employed. A third, similarly wounded, recovered, the antidote having been immediately administered. De la Condamine states that age and a low temperature lessen the activity of the poison.

Broeklesby† experimented on a cat with the woorara by inoculating the animal with it. The cat expired in about half an hour. An hour afterward the heart was pulsating, and it continued to beat for two hours after the animal's head was cut off. He found the poison to kill a small bird the moment two drops of it, in solution, were placed on the tongue. He also performed other experiments with it, which, however, do not possess any particular interest.

Herissant‡ instituted a great many experiments on animals with the woorara. Among others is one of, at first sight, considerable importance. He placed a tight ligature around the

* Relation abrégé d'un Voyage fait dans l'Intérieur de l'Amérique, Méridionale, etc. Mémoires de l'Académie des Sciences, tome lxii., 1745, p. 391 et seq.

† Letter to the President of the Royal Society. Philosophical Transactions, vol. xlv. part ii., 1747, p. 408.

‡ Experiments made on a Great Number of Living Animals with the Poison of Lamas and Ticunas. Philosophical Transactions, vol. xlvii., 1751-52, p. 75.

right posterior leg of a rabbit, and inoculated the animal with the poison of lamas and ticunas below the constriction. The rabbit died in less than ten minutes. In this case it is more than probable that a portion of the poison entered the circulation.

A bear wounded with an arrow dipped into a solution of the poison died in less than five minutes.

He also states that a small boy, to whom he had assigned the task of superintending the evaporation of an aqueous solution of the poison, became sick and faint, but recovered by exposure to fresh air and the administration of a pint of wine and a quantity of sugar. He was himself similarly affected, but recovered by like treatment.

From his experiments he concludes, among many other deductions, that the animals killed with the poison of lamas and ticunas are paralyzed in almost all the muscles before death, and that the muscles are pale and totally deprived of blood.

Fontana's* investigations were of a much more philosophical character than those we have referred to, and have formed the basis for most of the succeeding experiments on the subject. He showed conclusively that the vapor of the poison is not deleterious when respired, and thus dissipated one of the ridiculous ideas which had been circulated relative to its action.

Fontana's experiments are so admirably conceived and carried out, that we think it advisable to lay the main facts of some of them before the profession.

With reference to the action of the ticunas when taken internally, Fontana was the first, we believe, to point out the fact that the state of the stomach at the time of the administration of the poison exercises a most important influence over the result. Thus he found that when the animal's stomach contained a con-

‡ *Mémoire sur le Poison Americaine, appelée Ticunas, etc. Sur les Poisons et sur le Corps Animal. Florence, 1781, tome ii. p. 83 et seq.*

siderable amount of food, death did not follow; but that when this viscus was empty, the animal succumbed, though at a later period than if the substance had been inserted into a wound. Moreover, a larger quantity was required.

He also determined the inefficacy of acids and alkalies as antidotes to the action of the ticunas.

With reference to its effect upon the blood, Fontana found that coagulation was absolutely prevented when a solution of the poison was mixed with it, but that the red corpuscles were not at all modified either in form or size.

He next investigated the action of the ticunas when applied to a nerve entirely isolated from the surrounding tissues. After many careful experiments, he arrived at the conclusion that under such a condition no poisoning is produced.

From additional observations he finally concludes that the ticunas destroys the irritability of the voluntary muscles, but does not affect that of the heart.

We next come to Brodie's* researches, which were instituted with woorara brought from Guiana by Bancroft. It was found that after apparent death the heart continued to pulsate for some time, and that its action might be still further prolonged by means of artificial respiration. It was also further ascertained that after division of the nerves supplying the inoculated limb, or ligature of the thoracic duct, the effects of the poison were still produced if the circulation of the blood was not impeded; and hence it was concluded that it is only through this latter channel that the substance in question is capable of exercising its influence. Finally, it was determined that woorara affects the brain by passing into the circulation and acting directly upon the cerebral substance.

* Experiments and Observations on the different Modes in which Death is produced by certain Vegetable Poisons. Philosophical Transactions, part i., 1811, p. 178 et seq.

In a continuation of the paper quoted, Brodie* details the results of further experiments relative to the effects of artificial respiration on animals apparently dead from poisoning with woorara. In one case the animal was perfectly restored to life through the means referred to, notwithstanding the function of the brain had been entirely suspended for a long time.

Waterton† also has shown that by means of artificial respiration life may be preserved in animals poisoned with woorara.

Passing over a number of other observations on this subject to which we might refer, we come next to experiments of a later date, performed under more enlightened physiological views, and consequently with more definiteness of purpose. We shall present the main results of these in due order.

Virchow and Münter‡ are the first to whom we have to refer under this head. Numerous experiments were performed by these observers, from which they deduce the following conclusions:—

1. That the woorara, even after having been kept dry for five years, is still intensely poisonous.

2. That the physiological action of the woorara is in harmony with the chemical analysis which denies the presence of strychnia.

3. That woorara, therefore, does not belong to the class of tetanic poisons, but, like opium, induces stupor; and although it causes slight convulsive actions in cats, there is, nevertheless, neither tetanus nor trismus.

4. That it induces paralysis of the voluntary muscles, with, at the same time, long-continued action of the involuntary muscles, (heart, intestines.)

* Further Experiments and Observations on the Action of Poisons on the Animal System. Philosophical Transactions, part i., 1812, p. 205 et seq.

† Experiments with the Woorali Poison; *Lancet*. Also *American Journal of Pharmacy*, N. S. vol. v., 1840, p. 234.

‡ *Reisen in Britisch Guiana*. Von Richard Schomburgk. Band i. s. 456, (note.)

5. That woorara does not appear to produce death by absorption from the external surface of the body, but only when it is absorbed through a solution in the continuity of the animal tissues.

6. That in poisoning by woorara, coagulation of the fibrin of the blood ensues in the same manner as though the animal is killed by mechanical means; and that death takes place not so much from any direct result of the poison, but indirectly by its causing the cessation of the respiratory process.

Next in order of publication are the experiments of Bernard and Pelouze.* After detailing to some extent the history and physical and chemical properties of the woorara, it is stated that animals poisoned with this substance die without tetanic spasm, there being only a few slight contractions of the muscles of the skin, face, and body.

On examining the bodies of animals poisoned in this manner, it was found that there was a total annihilation of all the properties of the nervous system; the reflex movements were found to be altogether lost; and in animals dead but for a minute, and still warm, the nerves were as inert as though life had been extinguished for a long time. The blood was found constantly black, coagulated with difficulty, and had entirely lost the property of becoming red on exposure to atmospheric air. It is asserted, from these facts, that the action of the woorara is very similar to that of the poison of the viper; and that the analogy is still stronger from the circumstance that, like the latter, it may be introduced into the stomach with impunity.

Experiments were then instituted with reference to this last point. In the first place, it was found that when woorara was mixed with gastric juice, and the solution introduced into the circulation of animals, death uniformly followed. It is hence

* Comptes Rendus, tome xxxi., 1850, p. 534 et seq.

concluded that it is not from any alteration produced by the gastric juice that the poison is innocuous when introduced into the stomach. The other digestive fluids—the saliva, bile, and pancreatic juice—were likewise without effect upon the poisonous properties of the woorara. The inertness of the poison when ingested into the stomach was found to depend upon the fact that the gastric mucous membrane does not allow the toxic principle of the woorara to pass through it.

The following experiment is adduced as tending to establish this view:—

The fresh gastric mucous membrane of an animal, (dog or rabbit,) recently killed, was adapted to an endosmometer in such a manner that the mucous surface was on the outside. In the instrument was then placed a solution of sugar in water, and the whole was plunged into an aqueous solution of woorara. At the end of three hours, although endosmosis had been effected, as shown by the elevation of the level of fluid in the tube, it was proven that the liquid contained therein possessed no poisonous quality; showing that the active principle of the woorara had not been transmitted. It was, however, determined that by allowing the arrangement to stand for a long time, the mucous surface became so altered as to permit the endosmosis of the poisonous agent.

It was also shown that the mucous membranes of the bladder, the nostrils, and the eyes were likewise impenetrable to the active principle of the woorara, and that only one mucous membrane of the body—that of the air-passages—was capable of absorbing this substance.

Vulpian,* in common with MM. Bernard and Pelouze, also found that the nerves very soon lost their irritability, and that

* Comptes Rendus de la Societe de Biologie de Paris, tome i., 2d serie, 1854, p. 73.

the muscles remained excitable for a considerable period in animals poisoned with woorara. Contrary, however, to the results obtained by these last-named observers, he ascertained that the woorara, when introduced into the œsophagus or stomach of certain animals, as frogs, tritons, and toads, produced death. He also found that when thus administered, the heart continued to beat for two or three days, while all the nervous functions were entirely abolished. Hence he concludes that the heart is independent of nervous influence.

The experiments of Brainard and Green, to which we have already alluded, will be further considered under another head, as will also the numerous and ably conducted investigations of Reynoso.

In a paper read before the Physiological Society of London Cogswell,* among other conclusions, arrives at the following: That woorara is a poison when swallowed; that it acts primarily as a stimulant, and secondarily, or as it may be termed, specifically, as a sedative, paralyzing the functions of the nervous system both locally, when it is immediately applied to the body, and constitutionally after it enters the circulation.

We now come to Kölliker's† investigations, which for thoroughness and completeness have rarely been equaled. His conclusions are numerous, and appear to be deduced with his accustomed accuracy.

He found that the woorara acting through the blood destroyed the excitability of the motor nerves, the terminal branches losing their excitability in a few minutes, while their trunks did not become affected for an hour or two later. He is of opinion that the sensory nerves are little if at all affected.

* Lancet, March 3d, 1855.

† Physiologische Untersuchungen über die Wirkung einiger Gifte. Virchow's Archiv, Zehnter Band, 1856, s. 88 et seq. For conclusions, see also Comptes Rendus, tome xliii, 1856, p. 791, and Proceedings Royal Society of London, 1857.

When introduced into the system through the mucous membrane of the intestinal canal, Kölliker found the woorara to act more slowly than through a wound, and that a larger dose was required. When applied to the skin of frogs, he found it altogether inoperative.

With reference to its effect upon the heart, it was determined that in amphibia this organ was but little influenced, as it continued to pulsate for many hours after poisoning was established. Owing to paralysis of the pneumogastric nerves, it was somewhat quickened in its action. He concludes, therefore, that the ganglia remain unaffected. The lymph hearts soon ceased to move.

When applied locally to nerves, woorara in concentrated solution was found to extinguish their excitability, but only after a considerable time. Applied directly to the brain and spinal cord, it was altogether without effect.

The conclusions in regard to the effect of woorara upon the sensory and motor nerves, though published before those of Bernard* on the same point, are similar to those which the latter had previously announced in his lectures.

In a second paper, Vulpian details the results of further experiments with woorara. He confirms Kölliker's and Bernard's conclusions relative to its action on the nervous system.

He also investigated its effects upon the lymphatic hearts of frogs, and ascertained that under its influence they very soon ceased to beat.

Bernard's most complete researches relative to the action of the woorara are contained in the work to which we have already alluded. As this is so readily accessible to the members of the profession, we shall do no more than present the main results of his investigations. He found—

* *Leçons sur les Effets des Substances Toxiques et Médicamenteuses.*

1st. That all reflex movements cease a few minutes after poisoning, the heart continuing to beat for a considerable time.

2d. That woorara is not absorbed from the mucous membrane of the stomach during digestion, the bladder, or the conjunctiva of mammals, but is readily taken up from the pulmonary and rectal mucous membranes of these animals. When introduced into the œsophagus or gizzard of birds, it is speedily fatal. Applied to the dry skin of frogs, it acts slowly but surely. In contact with the wet skin of these animals, it is not absorbed.

3d. Woorara abolishes the function of the motor nerves, but does not affect that of the sensory nerves. Muscular irritability is rather augmented than diminished.

4th. That woorara kills the nerves from the periphery to the center, acting in this respect conversely to strychnia.

5th. That it causes death by arresting the process of respiration, thus inducing asphyxia.

The experiments of Prof. E. Pelikan,* of St. Petersburg, tend to conclusions similar to those we have last quoted. This observer, however, found that the nervous irritability did not always disappear immediately after death, as stated by Bernard. Prof. Pelikan also found that when introduced into the intestinal canal, woorara exercised its ordinary effect, though more slowly than when acting directly through the circulation. Curarin obtained by the process of Roulin and Boussingault produced the same physiological effect as the woorara.

Having thus brought the history, the chemistry, and the physiology of woorara to the present time, we come, in the next place, to speak of our own researches. These have been conducted with all the care which such observations require. Though we have worked to a certain extent independently, every experiment in-

* Physiologische und Toxicologische Untersuchungen über Curare. Virchow's Archiv, Elfter Band, 1857, s. 401. See also Comptes Rendus, tome xliv., 1857, p. 507.

stituted by one has been verified by the other, so that we are mutually responsible for the statements contained in this memoir. Moreover, observations and suggestions have been freely exchanged.

Original Researches.—The varietics of woorara which we propose to consider were brought, in February, 1857, from the Rio Darien, in the province of New Granada, South America, by Drs. Ruschenberger and Caldwell, of the United States Navy. By them they were presented to Prof. Joseph Carson, of the University of Pennsylvania, who very generously placed all in his possession at our disposal.

The woorara thus obtained is of two kinds: one, marked "*Woorara, variety Corroval*," is asserted to be the strongest arrow-poison; the other, labeled "*Woorara, variety Vao*," is not considered so powerful. So far as we are aware, these species of South American arrow-poisons have never yet been noticed by those who have written and experimented upon the subject.

Our friend, Mr. Trautwine, late chief engineer of the Panama Railway, informs us that the arrow-poison employed by the Indians of the Rio Atrato, on the eastern side of New Granada, is not at all powerful. He states that he has frequently wounded birds, pigs, and other animals with it without producing any marked result. The Indians, however, told him that they used a more virulent poison when they went to war; but if this be true, he was unable to obtain any of it. He has never heard them call any of their poisons by the name of corroval or vao.* In regard to the manner of manufacturing the varieties we refer to we have been unable to obtain as yet any information.

* Also Rough Notes, etc., by John C. Trautwine, C. E. Philadelphia, 1854, p. 65.

CORROVAL.

Physical and Chemical Characters.—The corroval, when in large lumps, is of a brownish-black color. Reduced to fine powder, it becomes a tawny yellow. The larger pieces have very much the appearance presented by vegetable extracts of the same color. Its taste is intensely bitter and very persistent. The saturated aqueous infusion is of a very dark-brown almost black color, and of neutral or exceedingly slight acid reaction.

Fig. 1.



The alcoholic tincture is of a pale-yellow tint. Both water and alcohol extract the active principle. The insoluble residue, viewed by the microscope, is seen to consist of vegetable cells, starch granules, and other vegetable structures, oil globules, etc. Small grains of silica are also to be observed. No parts of animals of any kind can be discovered, Fig. 1. It is very certain that these latter do not enter into the composition of corroval.

In the aqueous solution, when long kept, large colonies of infusoria are found, probably all of a vegetable character.

The aqueous solution mixed with blood does not retard its coagulation or alter the shape of the blood disks more than would any bland fluid of similar density. It is not at all poisonous to plants. We have inoculated tender flowers with it repeatedly without producing any effect upon them.

In order to separate the active principle from the corroval, the following processes were adopted:—

1st. Ten grains of the substance were extracted by repeated portions of boiling water, till a bitter taste was no longer afforded. The solutions were now mixed and boiled with magnesia. The whole was thrown upon a filter and the residue well washed with boiling alcohol. It was perfectly insoluble, showing, therefore, the absence of strychnia.

The filtrate was filtered repeatedly through animal charcoal, till all the bitter principle and coloring matter were absorbed. The charcoal was then treated with boiling alcohol in fresh portions till all bitterness was entirely extracted. The alcohol was then evaporated to dryness. By this process a greenish-white substance, insoluble in water, was obtained. It was readily dissolved by alcohol, ether, or chloroform. It is not crystallizable. It forms salts with hydrochloric, nitric, and sulphuric acids, none of which crystallize.

2d. The process employed in this instance was that used by Roulin and Boussingault, but modified by employing water to extract with instead of alcohol.

Ten grains of the corroval were reduced to fine powder and extracted with water, as in the first process. To the solution tannic acid was added, a voluminous flaky precipitate of a yellowish-white color was thrown down. This was well washed in a filter, to remove the tannic acid, mixed with water and heated to boiling, a few crystals of oxalic acid being added, till it was

entirely dissolved. The acid liquor was next treated with magnesia in excess, and filtered. The filtrate was evaporated to dryness, and the extract thus obtained dissolved in hot alcohol. This solution evaporated to dryness furnished a substance similar to that obtained by the first process, but more highly colored.

For the substance procured by the foregoing processes, possessing as it does all the qualities of an alkaloid, and in an eminent degree all the toxic properties of the corroval, we propose the name of *corrovalia*. We regret that we are unable, owing to the smallness of the quantity, to enter at present more fully into the chemistry of this interesting substance. From repeated observations we have, however, ascertained that it produces effects upon the animal organism precisely identical with those caused by the corroval itself, requiring, however, an infinitesimally smaller dose.

Physiological Investigations.—The action of corroval upon the animal organism is so entirely different from that of the ordinary woorara, as to indicate very strikingly its dissimilar composition. At the same time, the more obvious effects do not present any considerable variation. This is well shown from the following experiments:—

Experiment. A pigeon was inoculated near the cloaca with a little strong infusion of corroval. The bird at first exhibited no uneasiness. After the lapse of two minutes it walked a few steps, and began to show signs of discomfort. At the end of four and a half minutes it suddenly fell, flapped its wings once or twice, and died without further struggle.

Experiment. A large owl was inoculated with a small fragment of corroval in the leg. Owing to the density of the tissues of the part, or to some other cause, the poison was not absorbed after twenty-five minutes had elapsed. It was, therefore, again introduced, in solution, under the left wing. After three minutes continuous movements of the muscles of the throat were induced.

The bird staggered, let its wings fall, and appeared to stand with difficulty. About the end of the sixth minute it fell, and died without the least convulsive movement. The pupils were enormously dilated.

Experiment. A mouse was pricked with a knife charged with a solution of corroval. It fell dead in three and a half minutes, without the slightest spasm.

Experiment. Under the skin of a large frog a few drops of a strong solution of corroval were introduced. The animal remained, apparently, unaffected for twenty-five minutes; at the end of this period paralysis of the voluntary muscles commenced. When quietly laid upon the back, and the extremities stretched out, no effort was made to assume another position; when irritated, however, the extremities were withdrawn. The frog was entirely dead in forty-eight minutes—*i.e.* exhibited no motion of any kind to ordinary stimulus.

These experiments are sufficient to show the general effect and virulence of the corroval. It is perceived that, so far as these points are concerned, its action is very similar to that of the strongest woorara. There is no tetanic spasm, a fact which sufficiently proves the absence of strychnia. As we shall presently show, however, when the action of the corroval is more physiologically considered, many important points of difference between it and the ordinary woorara will be found to exist.

Action on the Heart.—The woorara hitherto used by experimenters was found, as we have already seen, to exercise little or no direct influence on the heart. This organ continued to beat in all animals for a considerable period, and, even after it had entirely stopped, it could be made to resume its actions by artificial respiration. The action of the corroval is in this respect directly antagonistic, as will be perceived from the following experiments:—

Experiment. A small frog was poisoned with corroval by

inserting a minute piece of the substance under the skin of the back. The chest was then opened, so as to show more distinctly the action of the heart. During the third minute after the insertion of the corroval the heart beat forty-five times, and very irregularly. For the fourth minute the pulsations were but thirty. During the fifth minute the ventricle acted in a very singular manner, small portions of its tissue being apparently paralyzed, and bulging out, while the rest was contracted. The pulsations were but eighteen. In five and a half minutes from the inoculation the ventricle had entirely ceased beating, and had contracted to a very small bulk. It was hard and rigid, and of a pale-red color, showing the entire absence of blood both from its tissue and cavity. The auricles continued to act for two minutes longer, when they also ceased. Instead of being contracted, the auricles were rather dilated. Galvanism was applied to the heart, without having the slightest effect in exciting it to action. The lungs or air-sacs were perfectly collapsed.

During the whole of this period the voluntary muscles were active. The frog struggled violently to escape, and finally succeeded in leaping to the floor. It remained active for twenty minutes. The pupils, which at the time the heart ceased to act were contracted, now became dilated, and all voluntary movements were abolished.

Experiment. A pigeon was inoculated with a little strong aqueous solution of corroval. It fell dead in five and a half minutes, without convulsive action. The pupils were enormously dilated. The chest was immediately opened, and the heart was found to have ceased pulsating. Under the influence of a powerful galvanic current a few fibres contracted two or three times. It was incapable of further excitation. The ventricles were somewhat corrugated, and the auricles dilated. The peristaltic action of the intestines was readily excited by galvanism for about half an hour.

Experiment. A rabbit was inoculated in the leg with a little

strong infusion of corroval. In three minutes the animal exhibited great uneasiness, and constantly moved the jaws, as if chewing something. In six and a half minutes it fell dead, without the least spasm of any kind. The pupils were largely dilated. The chest was immediately opened, and the heart was found to have ceased pulsating. The ventricles were small and empty; the auricle contained a quantity of dark fluid blood. A single ventricular contraction was induced by galvanism.

Experiment. The crural nerves of a very large frog were isolated, and a ligature placed under them and tied tightly so as to include all the tissues but the nerves. A large quantity of the aqueous solution of corroval was then injected under the skin of both legs. The chest was then opened, so as to show the movements of the heart. These did not seem to be disturbed, except by the impediment caused to the circulation by the ligature. After ten minutes the pulsations were forty-five per minute. At the end of half an hour the heart was still active, beating forty-eight times per minute. The ligature was now removed. The heart almost immediately began to exhibit the ordinary signs of the action of the corroval, viz., the partial paralysis and irregular contractions which it occasions; and in six and a half minutes the ventricle had entirely ceased to act. The auricles pulsated for two and a half minutes longer. No contractions could be induced by galvanism. Dilatation of the pupils ensued in twenty-five minutes, and all voluntary movements ceased.

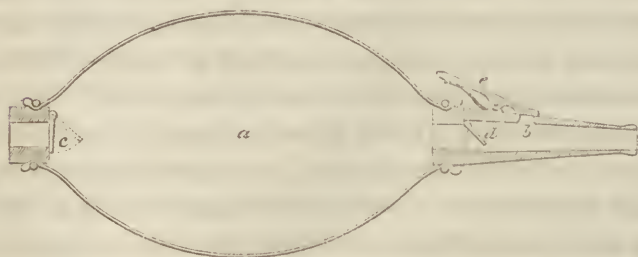
From the foregoing experiments relative to the action of corroval upon the heart, which have been frequently repeated, with uniform results, we arrive at the conclusion that it acts directly upon this organ by being carried to it through the circulation. It is well known that in cold-blooded animals the respiration may entirely cease, and the heart nevertheless continue its action for a considerable period afterward. These results, indeed, follow the poisoning of such animals by the ordinary woorara; and, as

Brodie, Waterton, and numerous other experimenters have shown, if the respiration be continued artificially in warm-blooded animals poisoned with this substance, life may be preserved; and even after the heart has ceased to act, it will again resume its movements under this influence. The discontinuance of the function of the heart through the action of the corroval must, therefore, be regarded as a primary effect, in no degree dependent upon the respiratory process, but due, as we have already stated, to the direct influence of the poison upon the heart itself. In order, however, to place the matter beyond doubt, the following experiment was instituted:—

Experiment. The trachea of a cat was opened, and a tube introduced, to serve for the attachment of an apparatus for conducting artificial respiration.* A quantity of strong infusion of

* The apparatus we have devised for the purpose stated, and of which a figure is annexed, has been found to answer very admirably, and can be

Fig. 2.



much more easily managed than the ordinary bellows. An India-rubber bag *a* has openings in both ends, into which two brass tubes are fixed, provided with valves *c d*. The tube *b* is attached to a tube of India-rubber, which, by a nozzle and stop-cock, is inserted into the trachea. When the bag is squeezed, the valve *c* is closed, and the valve *d* opening, the air passes into the lungs. On removing the pressure, and raising the valve *e*, the air escapes from the lungs through it, the valve *c* opens, the valve *d* closes, and the bag again becomes filled.

The instrument was made for us by Messrs. J. W. Queen & Co., 924 Chestnut Street, Philadelphia.

corroval was then injected under the skin of the flank, and the chest immediately opened. Artificial respiration was then instituted. The heart was actively pulsating. In a few moments its operation became irregular, and at length ceased entirely, seven and a half minutes after the introduction of the poison. The pupils, which at first were contracted, gradually became enlarged to their fullest extent.

The independence of the heart in relation to the respiratory process is thus fully shown, and one of the main points of difference between the action of the corroval and that of the woorara indicated. It is, perhaps, useless to bring forward further illustrations in support of the facts we have stated; but the following experiment is so apposite and conclusive that we cannot refrain from adducing it:—

Experiment. A young alligator, about a foot in length, was properly arranged, and the chest opened. The heart was beating thirty-six times per minute. A little solution of corroval was next introduced under the skin. The pulsations of the heart, five minutes afterward, were thirty-four per minute. The respiratory actions were vigorous, and perfectly effectual. After twelve minutes the action of the heart began to be irregular, and the pulsations had fallen in number to twenty-eight per minute. The rhythm of the auricles with the ventricle was entirely reversed, and the former was very curiously corrugated. The heart ceased acting (both auricles and ventricle) seventeen minutes after the inoculation. The left auricle was of a pale-red color, the right was black, the ventricle was pale and contracted. The heart stopped immediately after vigorous and long-continued respiratory movements. The lungs were well filled with air, and respiration was actively continued for sixteen minutes after the heart had ceased to pulsate. The pupils, which for a few minutes before the heart became affected were contracted to mere lines, were now dilated to a great extent, and all voluntary movements ceased.

From the foregoing experiments, we do not see how any other conclusion than the one we have stated can be adopted, viz., that the discontinuance of the heart's action is a primary result, and not due to the disturbance of any other function. Whether we regard the cause of its motion as being due to muscular irritability or to the ganglia found throughout its tissue, we cannot avoid the inference that both are powerfully influenced through the action of the corroval. In the experiment last stated we have seen that the rhythm of the heart was greatly disturbed, and that it continued to pulsate in the most irregular manner. We might adduce numerous other observations to the same effect. All this brings us to the conclusion that the ganglia are primarily affected, especially as from the contraction of the pupils and the cessation of the capillary circulation, to which we shall presently allude, we are led to infer the paralysis of the sympathetic nerves. No doubt, however, can exist that the muscular irritability of the heart is also completely destroyed, for no irritation, not even that of the strongest galvanic current, can re-excite its pulsations a minute after they have ceased; and even before the lapse of this short period we can obtain but one or two feeble manifestations of the force which once caused its throbbings.

We have as yet said nothing relative to the action of the corroval upon the *lymph hearts* of frogs. Without stating the experiments in full, we may say that, from frequent observations, we have convinced ourselves that under the influence of this agent they cease to pulsate in from twenty to thirty minutes after its introduction into the circulation.

We may here refer to the influence of the corroval over the *capillary circulation*. We have uniformly found it to be arrested one or two minutes before the ventricle stopped acting. We consider this to be due to paralysis of the sympathetic nerves.

While viewing the web of a frog's foot, in order especially to satisfy ourselves relative to the above point, we have never seen

any alteration in the size, color, form, or number of the red or white corpuscles. We have already, however, stated our views upon this subject.

The action of the corroval upon the *nervous system*, though in one or two respects similar to that of the ordinary woorara, is, we think, in others materially different. The latter destroys all voluntary and reflex movements immediately; it acts exclusively on the motor nerves, leaving the sensitive nerves unaffected, as Bernard has satisfactorily shown. As we have demonstrated, the first action of the corroval is directly upon the heart, and hence we have one important point of difference in the effects of the two poisons. In considering the action of this substance upon the nervous system, we shall indicate other points of dissimilarity.

1. Influence of Corroval upon the Voluntary and Reflex Movements.—*Experiment.* A large frog was inoculated with corroval under the skin of the back. The heart ceased pulsating in seven and a half minutes. The frog continued active for twenty minutes after the insertion of the poison, and at the end of twenty-five minutes all voluntary movements had ceased, paralysis first occurring in the anterior extremities. If now an extremity was irritated, it was immediately withdrawn, and galvanism applied to one foot excited movements in all the others. This condition remained for forty-five minutes after the introduction of the corroval, when it was changed, and reflex movements could only be excited in the nictitating membrane. In one hour and five minutes all reflex movements were lost.

Experiment. A young alligator was inoculated with corroval under the skin of the flank. The heart ceased acting in seventeen minutes, and in thirty-five minutes all voluntary movements were abolished, the anterior extremities first losing the power of motion. Upon pinching the tail, violent reflex motions were excited in all parts of the body, including the lungs, and strong respiratory movements were produced. They were readily ex-

cited for more than an hour and a half after the stoppage of the heart.

Numerous other experiments could be adduced to the effect above indicated, viz., that in cold-blooded animals the voluntary and reflex movements remain for a considerable period after the cessation of the heart's action, and consequently much longer than after poisoning with the ordinary woorara. At first sight it appeared to us that the abolition of these manifestations of the integrity of the brain and spinal cord, which eventually occurred, was due to the direct action of the corroval; but after the institution of other experiments; and a fuller consideration of the subject, we have arrived at a very different conclusion. In order to ascertain the effect upon the brain and spinal cord of the cessation of the heart's action, or, what amounts to the same thing, the prevention of the passage of the blood to or from them, we performed the following experiment:—

Experiment. The chest of a large frog was opened, and a ligature placed around the vessels at the base of the heart. All voluntary movements ceased in twenty-five minutes; and at the end of fifty-five minutes no reflex actions could be excited in any part of the body. The sciatic nerve of the left posterior extremity was exposed, and, on being irritated, strong contractions were produced in the muscles of the leg. This condition was present at the end of two and a half hours.

The experiment was frequently repeated, with uniform results. The voluntary movements always ceased in from twenty-five to thirty-five minutes, and the reflex in from fifty minutes to an hour and a quarter, after the ligation of the vessels. We consequently feel warranted in concluding that the cessation of these actions in animals poisoned with corroval is an indirect effect resulting from the cessation of the function of the heart, and therefore not due to any specific effect upon the brain or spinal cord.

2. Action upon the Nerves and Muscles.—The woorara, as

experimented with by Bernard, Köl liker and others, was found to immediately destroy the excitability of the nerves, leaving that of the muscles unaffected, or perhaps augmented. We have not found this to be the case with the corroval, as the following experiments will show:—

Experiment. A large frog was inoculated with a little strong solution of corroval. The movements of the heart were arrested in seven minutes. Voluntary motion ceased in about twenty-five minutes, and the reflex in about an hour, after the introduction of the poison. The sciatic nerves of both posterior extremities were now exposed. Upon gently pinching either of them, strong contractions were produced in the muscles of the corresponding leg. They remained excitable to galvanism for an hour longer. The muscles were irritable fifteen minutes after excitability was lost in the nerves.

Experiment. A cat was inoculated with corroval. Death followed in about five minutes. The sciatic nerve of the right leg was exposed, and, on irritating it, strong contractions were produced in the muscles of the extremity. The nerve continued irritable to galvanism for twenty-six minutes after death, the muscles for thirty-five minutes.

Experiment. A pigeon was killed with corroval, death ensuing four minutes after the introduction of the poison. The sciatic nerve was irritable for seventeen minutes subsequently. The muscles retained their irritability for twenty-two minutes.

From these experiments we see that nervous excitability remains for a longer period than in cases of poisoning with woorara. This function is nevertheless affected by the corroval, for, as we have seen, it remains much longer present in animals whose circulation has been arrested by ligature of the large vessels. Consequently the mere deprivation of oxygenated blood, or the retention of that which is not decarbonized, cannot be the cause of its abolition, and we must, therefore, ascribe it to the direct action of the poison.

We also perceive that the muscular irritability was lost very soon after that of the nerves, and consequently we have here another point of difference with the woorara. It may perhaps be thought, by those who disbelieve in direct muscular irritability, that the reason why the muscles appeared irritable after the loss of excitability in the nerves was due to another cause, viz., the retention of this faculty in the minute ramifications of the nerves after its loss in the larger trunks. In relation to this point, we think we can show that the corroval, like the ordinary woorara, causes the death of the nerves from the periphery to the center, and consequently that the minute ramifications lose their vitality before the larger trunks. In illustration we subjoin the following experiment:—

Experiment. A few drops of the strong infusion of corroval were introduced under the skin of the back of a large frog, the sciatic nerve of the left side having been previously cut. The heart ceased to act in eight minutes—voluntary and reflex movements ceased respectively in thirty and fifty-five minutes. The sciatic nerve of both sides were excitable, the left in a less degree than the right. After the lapse of an hour and a half, the left nerve had entirely lost its irritability, while the right was still excitable, and remained so for twenty minutes longer.

With strychnia, however, the effect is far different, this substance destroying the nervous excitability from the center to the periphery, as the following experiment shows:—

Experiment. Under the skin of a large frog, whose left sciatic nerve was previously divided, a few drops of a strong solution of strychnia were introduced. Tetanic spasms ensued in two minutes. After forty-five minutes the nerves were irritated by galvanism. That of the left side, which had been cut, responded energetically, while no motions could be produced through the uncut nerve. The former remained excitable for two hours later. Muscular irritability was strong in both legs. The experiment was not further pursued.

We infer from the foregoing experiments that the irritability of the muscles is a faculty entirely distinct from the irritability of the nerves, and that accordingly it may be present after the entire abolition of the latter. The fact that the corroval destroys the excitability of the nerves from the periphery to the center, acting first upon the small branches, and subsequently upon the larger trunks, is, we think, abundantly shown. Hence the contractility exhibited by the muscles on being galvanically irritated could not be due to excitability remaining in the minute nervous radicles.

With reference to the effect of woorara upon the sensory and motor nerves, it was found by Bernard and Kölliker that the latter first lost their vitality, the former not being directly affected. By confining the action of the poison to certain portions of the body, Bernard obtained movements in a non-infected limb by irritating one that was fully poisoned. Hence he proves that the woorara does not affect the integrity of the sensory nerves. We have performed his experiments frequently, substituting corroval for woorara, without obtaining his result. They are as follows:—

Experiment. The vessels of the left posterior extremity of a medium-sized frog were ligated, and all the tissues, with the exception of the sciatic nerve, divided. The limb was consequently only connected with the body through the medium of the nerve. The animal was then inoculated with corroval high up in the back. The movements of the heart were arrested in six minutes—voluntary and reflex movements ceased about the usual time. On irritating either of the anterior extremities, or the posterior leg which was not cut, no motions were excited in the left posterior extremity, showing, therefore, that sensation was entirely destroyed by the corroval. The irritability of the muscles subjected to the influence of poison was lost in one hour and fifty minutes after the inoculation, while it was present in the non-poisoned limb sixteen hours afterward. The animal was not further observed.

Experiment. The sacrum of a large frog was carefully removed, and the sciatic nerves isolated by passing a ligature around the body so as to include all the tissues but the nerves in question. This was tightly drawn and tied so as effectually to prevent the circulation of the blood in the posterior extremities. The frog was now inoculated with a solution of corroval in the manner last stated. The heart ceased to act in six and three-quarter minutes—voluntary movements were abolished in thirty minutes, and all reflex actions were lost in fifty-three minutes after the introduction of the poison. Strong galvanic irritation was now applied to the anterior extremities, and although muscular contractions were induced in them, there were no reflex movements in the posterior extremities. The sensory nerves had therefore lost their faculty of conveying impressions. Muscular irritability was extinct in all the anterior portions of the body at the end of two and a quarter hours. The muscles of the posterior extremities retained their irritability for twenty-two hours. The experiment was not further continued.

From these experiments it is perceived that the corroval, unlike the woorara, destroys sensation, and that so far from augmenting the irritability of the muscles, this faculty as also annihilated.

Bernard found that in animals poisoned with woorara, the muscles were red as if they contained a considerable quantity of blood. In all cases of corrovalic intoxication, the reverse is the fact, provided of course that the circulation has not been mechanically impeded by ligatures, etc.

Absorption of Corroval.—Corroval is readily absorbed from the mucous membrane of the stomach, and from the external surface of the skin of frogs. The following experiments are cited in illustration of this point:—

Experiment. Ten drops of the strong solution of corroval were placed in the stomach of a large frog. The chest was then opened. The heart was pulsating fifty times per minute; in a minute or

two afterward, the contractions of the ventricle became very irregular, the partial paralysis was present, and it ceased to act in five minutes after the introduction of the poison. The auricle stopped two and a half minutes subsequently. Slight convulsions of a clonic character now appeared in the posterior extremities, and lasted for a few minutes. The ordinary symptoms of corrovalic intoxication then ensued in regular order.

We mention it as a singular circumstance, that in all cases in which we have given the corroval internally, there were convulsive movements of the posterior extremities as above, while we have never seen them in frogs where it was introduced directly into the circulation.

Experiment. Ten drops of the strong solution of corroval (twenty grains to the ounce) were placed upon the back of a large frog. After the lapse of fifteen minutes the chest was opened. The heart was still pulsating actively. After ten additional minutes five more drops were placed upon the back—in a short time it began to act, and thirty-five minutes after the first introduction of the poison the heart ceased beating. The other consequences followed in due succession.

We deem it unnecessary to enter more fully at this time into the discussion of the questions connected with the absorption of the poison, or to bring forward other experiments. They will be considered at length under another division of our subject.

From the foregoing experiments and observations in relation to the corroval, we deduce in the main the following conclusions:—

1st. That it differs essentially from any variety of woorara hitherto described, both in its chemical constitution and physiological effects.

2d. That it acts primarily upon the heart, through the medium of the blood, producing an arrest of the action of this organ.

3d. That the annihilation of voluntary and reflex movements is a secondary result of its action, depending primarily upon the discontinuance of the function of the heart.

4th. That it acts upon the nerves from the periphery to the center, and abolishes both the sensory and motor functions.

5th. That it destroys muscular irritability.

6th. That it paralyzes the sympathetic nerve, this being one of its primary effects.

7th. That it is absorbed both from the intestinal canal and skin of frogs.

8th. That its poisonous qualities are due to an alkaloid hitherto undescribed.

VAO OR BAO.

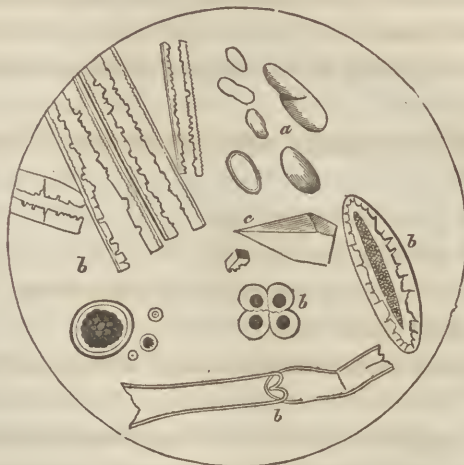
We shall now proceed to consider, in order, the physical, chemical, and physiological characteristics of vao.

Physical and Chemical Characters.—The vao in our possession is a dark-brown extract, perfectly dry and hard, and unaffected by exposure to the air. It is partially soluble in water and alcohol. The insoluble portion consists of a white or light-gray deposit, of a shred-like and flocculent appearance. Examined under the microscope, this is found to be principally amorphous matter with a considerable admixture of starch-cells, Fig. 3, *a*, and various forms of entire or broken cells, all of vegetable origin, *b*. A few broken crystals are also found, *c*, but no indications whatever of the presence of any relics of animal tissues, such as we should naturally look for were snake-heads and ants employed to make up this deadly material. The solutions of vao are of a tawny-yellow hue, and are feebly acid.

In the chemical examination of vao, the same processes were employed as were resorted to in analyzing corroval, and an alkaloid was obtained, which differed in no essential physical or chem-

ical character from that of corroval. When, however, equal quantities of corroval and vao were analyzed, the latter material yielded the smaller amount of alkaloid. The result of the physiological comparison of the two substances extracted from the poisons in question will be found elsewhere.

Fig. 3.



Before proceeding to study the effect of vao upon the tissues and organs, it will be well to present a general view of the symptoms and appearances offered to the eye by an animal poisoned with it, reserving their interpretation for after consideration.

Experiment. A morsel of vao was introduced under the skin of the belly of a large frog. No remarkable symptoms were noticed during the first twenty-seven minutes. The frog leapt about as usual, making violent efforts to escape from the receiver. At the close of this time his fore legs were weak. Twenty minutes later the hind legs were also weak, and although he remained in any unusual posture in which he might be placed, he still retained the power to move, apparently at will, and when irritated. Fifteen minutes later all volitional control had departed in the

extremities, although he retained the power to lift his head, and exhibited reflex motions of one leg when the other was irritated. At the close of the next hour the reflex acts ceased, the eyelids being the last muscular part which responded by reflex acts to external applications. Three hours and fifty-seven minutes elapsed between the inoculation of the vao and the loss of motor power in the lids. It is also to be observed that the frog continued to use the respiratory muscles of the lower jaw, and more rarely of the flanks, some time after he had lost all voluntary control of the extremities.

The order of externally visible phenomena is therefore as follows:—

1. Loss of power in the fore legs.
2. Loss of power in the hind legs.
3. Loss of reflex manifestations in the extremities.
4. Respiratory efforts cease.
5. The eyelids are no longer irritable, and do not close when touched.

In a few cases the frogs also exhibited convulsive motions, the hind legs being extended with considerable force, but not remaining rigid in this posture, as occurs when strychnia has been used.

When a warm-blooded animal, as a rabbit, is the subject of the action of vao, no marked symptom is observable until the head begins to droop and the animal crouches on his belly at the close of about twenty minutes. Before this occurs, there is sometimes noticed a chewing movement of the jaws and some gritting of the teeth, a symptom which is often well marked in rabbits poisoned with tincture of *veratrum viride*. At the close of fifteen or twenty minutes, as we have said, the head begins to sink, is jerked up, falls lower, is again jerked up, and at last is no longer lifted. Meanwhile the animal falls over on his side. The respiration becomes weaker and less frequent. The heart beats more slowly.

Slight convulsive motions of the ears and hind legs occur. The pupil, previously contracted, dilates, and in some cases the muscles of the skin are affected with a general movement. At last the respiration ceases, and the lids are no longer irritable. Meanwhile the heart is still acting feebly, and the temperature has fallen. After death the pupil contracts, and post-mortem rigor succeeds at an interval of from one to five hours.

The time required to destroy a rabbit is usually about half an hour or forty minutes, when the poison is introduced under the skin. Pigeons similarly treated die within fifteen minutes.

It will be seen from these statements that vao poison acts less rapidly than corroval, or the ordinary woorara of European observers. And this was even more manifest in the case of a cat whose symptoms differed very remarkably from those already described.

Experiment. A large black cat received in the thigh a lancet-point charged with dried vao. After two minutes the instrument was withdrawn, and found to have lost most of its poison. During thirteen minutes the animal showed no marked signs of the action of the vao, except a tendency to rest couched on her breast, and some indisposition to move about. Two minutes later she rose to her feet and made the same motions of swallowing and chewing which we have noticed in the rabbit. These proved to be the first symptoms of a violent vomiting which followed almost immediately. This action accomplished, the cat again rested on her belly, her head drooping as before, until after eleven minutes had passed, the chewing movements began again, and another violent attack of vomiting brought her to her feet. On this occasion only a little mucus was rejected. The head again sunk as she lay down, the respiration became short and quick, and the heart beat more slowly. Forty minutes after the vao was used she could still raise her head, and the eyes followed the motions of a candle passed to and fro in front of them. In the next five

minutes the head fell on one side, and the body rolled over a minute later, the pupils dilating to their utmost extent. Fifty-five minutes after the vao was given, the cat died in the most frightful general convulsions, with foaming at the mouth, vomiting, and ejection of urine and feces.

The difference between the external symptoms in this animal and the rabbit is as great as the effect produced on one and the same species of animal by two dissimilar poisons.

M. Bernard has never seen vomiting caused by woorara, but we cannot find that he has experimented with cats.* Virchow had already noted the fact that the cat is subject to convulsions when poisoned with woorara, and in this respect the vao poison resembles it. Cats are, however, so liable to convulsions that almost all poisons produce them, and very trivial causes will bring them on in kittens apparently in health. Thus we have seen a cat frightened into wild epileptiform convulsions.

Absorption.—In this connection it is still to be held in mind that the variety of woorara poison which we have now in view is far less active than the woorara examined by Bernard and Köl liker, and even less so than the corroval of which a portion of our paper treats.

The phenomena which announce the absorption of the vao are therefore slower in appearing, and have sometimes to be awaited a considerable time. The actual length of time required for absorption to occur is, however, of less moment than the facts relative to the absorbing power of the various tissues with which the poison may be placed in contact, and the exterior circum-

* The chewing movement which we have described as preceding the act of emesis in the cat, was also noted in nearly all of the warm-blooded animals poisoned with either corroval or vao. In one of them (a pigeon) vomiting took place. It is possible that the peculiar movements alluded to may be indicative of the existence of nausea which does not reach the actual climax of vomiting.

stances which seem to be influential in determining the rate of absorption.

Most of our experiments have been made upon frogs. We shall detail the results with reference to the various tissues.

Areolar Tissues.—When a morsel of vao was placed under the skin of a frog death inevitably ensued, whether the animal was left in dry or moist air, or in water, and no important difference was observable in these several cases, save that when a solution was employed the death was more rapid than when the solid poison was used. Thus, a frog of middle size received under the skin of his back a morsel of vao. In four hours all motion, voluntary and reflex, had departed. A second frog, of rather larger size, having received in one of its subcuticular sacs the same amount of vao dissolved in water, perished in forty minutes.

The same general rule applies to those warm-blooded animals upon which the poison was tried. An equal amount of vao being placed under the skin in two rabbits of about the same size, the one which received the vao in solution perished in eighteen minutes, while the other lived for half an hour.

Absorption by the Skin.—Vao, like woorara, is best absorbed by the skin of the frog, when the skin is comparatively dry, a fact which was first observed by M. Bernard, and which he conceives to be owing to the constant exhalation of a viscous and protective mucus, which is abundant when the frog is in, or just removed from the water, and which is scarcely observable when the frog has been long out of that element. The following experiments sufficiently illustrate these facts with reference to vao:—

Experiment. A large frog, which had been kept under a receiver open at top during several days, was found to have a skin much less lubricated than that of a frog kept in water. The skin at the middle of the back was cleaned with a piece of cotton wadding, and a small portion of a paste composed of vao was put upon the spot thus deprived of its mucus. The frog being

replaced in the receiver, at the end of seven and a half hours all motion was lost.

Experiment. A frog of smaller size was so imprisoned in a net of wire that he remained with about half of his body under water. Upon his back was put a smaller amount of vao paste than was used for the last frog, but the situation chosen was the same, no attempt being made to rub off the mucus. Although the vao was twice renewed within forty-eight hours, no accident resulted to the animal, nor was he to appearance in any way affected by it.

That, however, the amount of absorbing surface exposed to the action of the poison may modify the result very materially, was seen in the following experiments:—

Experiment. A small but very active frog, which had just been removed from the water, had one leg imprisoned in a piece of thin caoutchouc tubing, which was well filled with cotton saturated with an aqueous solution of vao—one grain to the ounce of distilled water; a morsel of the solid poison was also thrown into the tube, and the open end closed with slight pressure around the leg, above the knee. At the end of four hours and forty-five minutes, reflex motions were no longer to be excited by galvanism.

Experiment. The last described experiment was repeated with the single variation of placing the frog half under water, taking care to keep out of the water the leg which was in the tube and surrounded by poison. At the close of five hours no effect was visible. At the end of twenty-five hours the frog was sluggish; three and a half hours later all movement, reflex and voluntary, was over.

These two experiments, with others of a like character, seem to show that when a large amount of surface is exposed to vao in solution, and but half of the remainder of the body placed in water, absorption may occur; the same result being attained in a

far shorter period when one leg being kept moist with vao, the rest of the body is exposed to the desiccating influence of the atmosphere.

Now that the production of mucus does protect the frog to some extent, cannot be doubted, and has been proved by M. Bernard with his usual experimental skill. It will be seen, however, from the next set of experiments, that the amount of moisture in the system of the frog has much to do with his power to absorb the vao in solution, so that it is not only the exudation of mucus, but also the excess of watery supply which enfeebles the absorptive process. When the frog is dried more or less by long exposure to the air, his body eagerly takes up the moisture which is presented to any part of the surface. When, on the other hand, his body is thoroughly moistened, and the supply of water is in contact with the larger part of his surface, the power to absorb an aqueous fluid of a higher specific gravity than water from any one part of the surface is considerably lessened. Of course the presence of water is essential to the production of the viscous mucus, which is supposed to be the means of protecting the wetted frog, but it is also probable that the varying supply of water regulates the rate of absorption of aqueous solutions placed in contact with a part of the skin, or, as we shall now show, in the interior of the digestive canal.

Absorption from the Digestive Canal.—*Experiment.* A small frog received in his stomach thirty drops of a solution of vao, one grain to the ounce of water. The dose was given through a glass tube, whose edges were carefully rounded that the mucous membrane might not be wounded. None of the poison escaped. The frog was placed on a damp cloth in a receiver containing a wetted sponge. At the end of nineteen hours and fifteen minutes he was found to be inert and sluggish, though still able to raise himself when suspended by one leg. In twenty-two hours longer he was unable so to lift himself. Seven hours later all motion

had departed—the naked muscles were feebly irritable to galvanic stimulus, and the heart beat in successive minutes 2, 2, 2.

Experiment. A second frog which had received the same dose in the same way, and at the same time, and which had also been placed in like circumstances, died during the ensuing night.

Experiment. A small frog received thirty drops of the same solution and was at once placed in water. At the end of four days he was perfectly well.

Experiment. Two small frogs received each of them thirty drops in the stomach, and were placed together in water. No. 1 lost all reflex and voluntary motions at the close of twenty-four hours. On examination no sufficient cause could be found to explain his early death. No. 2 was well and active after five days.

Experiment. A small frog received in his mouth a morsel of vao, which he twice rejected; it was finally placed far back and to one side. He was then left upon paper that the poison might be seen if again rejected; a large receiver was then placed over him and he was left to himself at 12 M. He died during the ensuing night.

It follows from these experiments that vao in the dose here stated is poisonous to frogs when placed in the mouth or when directly carried into the stomach. It will also be observed that the frogs which, after receiving this dose, were placed in water, suffered but little—one out of three perishing within four days, while frogs of the same size who were treated in like manner, except that they were confined in an atmosphere more or less dry, one and all suffered from the poison. Still, as it was possible that the frogs which, being placed in water, survived, might have rejected the poison, or diluted it largely and frequently by swallowing the water in which they were placed, it became necessary to test this negative result.

Experiment. Accordingly a frog of middle size received in his stomach by a tube thirty drops of the one-grain solution. Three

wire ligatures were next carried through the skin of the upper and lower jaw, at a little distance from the lips, and firmly twisted, so that no water could easily enter or leave the mouth. Thus prepared, the frog was suspended in water, his head alone remaining above the surface. At the close of the second day he was rather sluggish, but on being released and allowed to remain at liberty for a time he did not seem to have been materially affected. Replaced in the water, he was observed at intervals up to the close of the fourth day, when, as he seemed in nowise the worse for the poison, he was set free, and the observation ceased. It is not, therefore, direct dilution with water which renders the ingested poison so harmless to frogs kept in that fluid.

The power of different parts of the intestinal canal to absorb the vao poison was also the subject of numerous experimental tests. The stomach was the organ first essayed, and to try its absorbent powers, we utilized a fact in the physiology of the frog which has been known to one of the authors of this paper for some time, but which we do not find elsewhere referred to. Under certain circumstances, a detailed account of which will be found in a note, the frog can be made to evert first the œsophagus and then the stomach, so that it is literally turned inside out, and projects from the mouth, its internal or mucous coat being exposed to the air.*

* Some time since, one of us (Dr. Mitchell) observed that when an irritating substance, such as tinct. *veratrum viride*, is poured into the mouth of a frog, the animal sometimes, by a sudden effort, everts the œsophagus, and then the stomach, so that the mucous surface of the latter organ projects from the mouth. If the frog be left to himself, he remains rather sluggish for a time, and finally returns the viscera to their usual places, apparently none the worse for this extraordinary performance. Suspecting that the pressure upon the abdominal walls, which cannot well be avoided when holding a frog, might have been influential in forcing the stomach out at the mouth, an attempt was made to produce the result in this manner alone, but without success. Since these facts were observed, Dr. James Darrach informs us that he has twice seen frogs who had thus everted the viscera

Experiment. A large frog thus prepared received on his everted stomach a morsel of vao made into a paste with a little water. A portion of the mucous membrane of the œsophagus at some distance was then secured in the grasp of a Liston forceps, and the shank of the handle slipped over a nail which was driven into the table. One of the fore feet of the frog was next secured by a wire so that he could not return the viscera to the belly again. A morsel of vao being placed on the surface of the stomach, he ceased to move in ten hours.

Experiment. In this case the lower jaw-bone was divided on both sides, so that he would be unable to aid himself by forcing the stomach into place again. Notwithstanding this precaution, the frog reverted his stomach after the lapse of some hours, but not before he had exhibited indubitable signs of being poisoned. He died within twenty-four hours of the administration of the vao.

Experiment. Two frogs were similarly treated, except that no vao was placed upon the everted organ, and that in one case the stomach was transfixed with a needle and thus retained in its strange position during twenty-four hours. The other frog restored the viscera to their places within two hours. When the needle was withdrawn from the stomach of the first frog, he made no immediate effort to replace his organs. Being put in water he seemed sluggish, but on examination next day proved to have succeeded in rearranging his disturbed anatomy. Both frogs were well three days later.

while in water and at perfect liberty. At all events, it is very difficult by any management, short of the means first mentioned, to obtain this result, without the co-operation of the frog. It is probably a mode of vomiting, and a normal physiological act. For purposes of experiment, such as those described in the text, the stomach may be everted by firmly pressing the belly with one hand, and with the other passing into the stomach a thermometer with a bulb larger than the stem. As this is withdrawn, partial eversion of the organs occurs, and may be made complete by a little manipulation with a pair of forceps carefully used.

In these experiments the stomachal mucous membrane was rather dry, and the whole organ much congested. The effect was less rapid than in the following experiment, where no doubt the local circulation was less interfered with :—

Experiment. The abdomen of a large frog being opened, the stomach was drawn out, and a ligature tied around the pyloric extremity. A morsel of vao was next slipped into the stomach through a slit in the œsophagus, and ligatures placed about the cardiac end of the viscus, and about the œsophagus above the wounded part, which was carefully excised. The vao acted fatally within two hours, an unusually sudden effect to be produced by this mode of using it. Lest a minute portion of the vao might have been left upon the wounded œsophagus, the experiment was repeated, with the variation of using a small tube through which the vao was carried into the stomach without opening the œsophagus, which was, however, tied just above the stomach. Poisoning took place in this experiment within five and a half hours. The frogs used had been just removed from water, and were afterward left under bell-glasses, as usual. Still, the effect was rapid. On examining the stomachs after death, we could not see that the ligatures had cut the internal coat, although they undoubtedly did bruise it, and perhaps imperceptibly tore its delicate surface.

Absorption by the Mouth and Oesophagus.—*Experiment.* The belly of a frog of middle size having been opened, and the œsophagus tied, the wound was closed, and a morsel of vao placed in the mouth. At the close of eighteen and a half hours he was active and well; a little jelly-like mucus could be seen at the back of his throat, tinged with the dissolved vao. Five and a half hours later his fore legs were feeble, and he could no longer lift himself by one leg when held suspended by it. Twenty hours later he was found devoid of motion in his limbs. The nerves were no longer irritable, but the heart beat 3, 3, 3 in successive minutes.

Experiment. A small frog was poisoned by the subcutaneous administration of the vao, which was still found after death, dissolved, in the buccal mucus of the subject of the last experiment. The mucus, therefore, does not alter the poison.

Absorption by the rectum takes place both in frogs and higher animals with considerable ease.

Experiment. A morsel of vao, placed in the rectum of a small frog, produced death within thirty-nine hours.

Experiment. A very large frog was opened, and the rectum divided. A morsel of vao was passed through a tube into the lower segment of the rectum, and ligatures were cast about the cut ends of the intestine, which was finally returned to the abdomen, and the wound sewed up. The frog was left under a bell-glass containing a damp sponge. He was not observed until twelve hours had elapsed, when he was found dead; the heart not beating, and the muscles scarcely irritable by galvanic stimulus. No trace of the poison could be seen in the rectum, except a small white shred, like the undissolved portion of vao which forms the sediment in its aqueous solutions.

Experiment. A small rabbit, into whose rectum was thrown an injection of vao containing about one-eighth of a grain, perished within one hour, notwithstanding that he had rejected a large part of the poison.

The vao poison is, therefore, readily absorbed by the rectal mucous membrane, as was also found by other observers to be the case in their own experiments. It follows, as a general deduction from our researches upon the absorbing power of the various tissues for vao poison, that the rectum, stomach, and mouth in the frog are all capable of admitting the poison to the system through their mucous surfaces; absorption by the skin or stomach being governed, as to its rapidity, by the needs of the system for aqueous fluid.

The subject of absorption was further studied in warm-blooded

animals, to ascertain whether the state of the stomach and system would affect the activity of the poison. It has already been mentioned, in the early part of this essay, that Fontana and Bernard had noticed that during digestion woorara could be ingested with an impunity which did not exist in the fasting animal. This statement we have found to hold good as regards rabbits to which vao had been given during a fast or during digestion. Those who were not digesting always died. This is the more curious because the stomach of the rabbit is never empty, and the mere fact of the mixture of the poison with the food cannot therefore be supposed to be the protective influence. M. Bernard finds an explanation of these curious facts in the circumstance that woorara, placed in contact with the outer wall of the mucous coat of a fresh stomach, will not pass through it to a solution of sugar on the other side of the membrane. The water in which the woorara is dissolved alone endosmoses to the syrup, and the poison is left behind. It is to be presumed that the mucous coat of the fasting stomach would permit of the passage of the poison; but as M. Bernard does not tell us in what functional condition were the stomachs when removed for his experiments, we are still somewhat in the dark.

It may be well to remark, in confirmation of M. Bernard, that the rule of protection is not absolute and without exception in animals who are digesting, since, when large doses—as one-fourth to one-half a grain—of vao are used, a death sometimes occurs even where a full meal has been previously taken.

Two very interesting experiments were made to ascertain whether the condition of the system of the rabbit, as regards water, would be found to modify the facts just stated.

Experiment. At different periods two large rabbits were kept on hay and corn, and without water, for nine days. At the close of that time, they were deprived of food during twenty-four hours. A feed of hay was then allowed them, of which they ate greedily.

An hour and a half later in one case, and two hours later in the other, they were obliged to swallow respectively one-fourth and one-half a grain of vao broken into coarse powder. They were then allowed to drink freely. Neither animal suffered. One of them was killed three days afterward, by introducing a minute morsel of vao under his skin. The other (seven days later) is still alive. We regret that our engagements oblige us to defer the fuller consideration of this interesting subject to another occasion, when we hope to be able to offer to the profession a more satisfactory explanation of the facts above stated than has been hitherto given.

Circulation and Respiration.—The following statements of experiments upon the effects of vao on the cardiac and respiratory movements are selected as illustrations from upwards of twenty separate records of distinct experiments upon frogs and warm-blooded animals:—

Experiment. A frog of middle size was selected, and the heart exposed by cutting out a triangular piece of the front of the thorax. His heart was beating forty-eight per minute, and with great regularity. After a short lapse of time, to permit any excitement consequent upon the operation to subside, the pulse was again noted at forty-eight, and a morsel of vao was placed in a small cut in the liver. In fifteen minutes the heart pulse fell to thirty-two. Three minutes later it was twenty-seven. Again, in three minutes longer the ventricle, after some irregular movements, ceased to act. Five minutes later the auricles were beating three times a minute, and the respiratory motions of the under jaw continued. Forty-seven minutes from the time at which the vao was inserted the auricular motions also ceased. The respiratory efforts were still visible, although very feeble. The heart responded to the galvanic stimulus for upward of twenty-five minutes. After the heart had ceased to act the frog leaped about actively, and seemed in no respect the worse for the operation until a longer period had passed by.

Experiment. A large frog received a morsel of vao under the skin of its back. At the close of forty minutes we exposed the heart. It was beating twenty per minute. Ten minutes later the auricles alone acted, and shortly afterward all motion ceased, although the frog was still active. The auricles continued to respond to galvanism, by single beats, during another half hour. At this time the nerves and muscles were still irritable to mechanical stimulus and to that of galvanism.

Experiment. A small frog received in his back a morsel of vao. At the close of an hour his heart was exposed; the ventricle beat feebly ten per minute. Ten minutes later the auricles alone moved. Again, in five minutes these also were at rest, although the whole heart responded well to galvanization during forty minutes longer. The nerves continued irritable some time after the heart ceased beating, and the muscular irritability elsewhere survived that of the heart.

Experiment. A large frog was poisoned by injecting a solution of vao into the subcuticular sac of the belly. At the close of one hour, and while he was still active under stimulus and restive when held, the heart was exposed. It beat twenty-nine per minute. Twenty minutes later the auricles alone acted, though the ventricle responded to galvanism by single pulsations. The auricles were at rest after eight minutes more had passed, and when the extremities were becoming affected by the vao. The auricles continued to act feebly when galvanized at intervals during the two succeeding hours, and while the nerves had entirely lost their irritability under stimulus of any kind.

The general muscular irritability long survived that of the heart. This organ was somewhat distended, the left auricle being loaded with blood, and the ventricle being also full and dark from the blood within it.

In six frogs, similarly treated, the auricles remained irritable under galvanic stimulus during periods which varied in the dif-

ferent cases from thirty minutes to five hours; while in other instances, and especially when the quantity inoculated was large, the heart refused to respond to galvanism so soon as its rhythmic action was at an end.

It will be seen from the cases here recorded that the heart usually ceased to pulsate before either nervous or muscular irritability was lost, and while the animal remained capable of all the usual voluntary motions. This is so remarkable in some instances that the frog was seen to seek a place of refuge, insinuating himself under the ledge of a test-tube rack, or hiding in the folds of a cloth left on the table.

The remaining observations upon the heart's action were made incidentally while studying the absorption of *vao* with reference to the various surfaces. Upon comparing these with the results last obtained, a very remarkable fact was observed with reference to the departure of irritability in the nerves and muscles, and the continuance of a pulse in the heart.

Since these experiments are stated more or less fully in the portion of this paper which treats of the absorption of *vao*, it is unnecessary to detail more than the facts which relate to the points in question.

In the cases alluded to, *vao* was administered to frogs by the skin, the stomach, the rectum, etc., as has already been described. Under these circumstances the phenomena moved slowly, and death was postponed as late as twenty-four hours or more after the use of the poison. It was then observed that in some instances the heart still acted, though with great feebleness, after all movement had departed from the voluntary muscles. When it did stop, the irritability was very rapidly lost.

In warm-blooded animals the heart usually continued to beat for a short time after respiration had ceased. As usual, the ventricle stopped first, and the auricles next. In a cat the heart beat for fourteen minutes after respiration had been checked, and was irritable under galvanism for a few minutes longer; though

in warm-blooded animals generally, who die of vao, this is not the case. In all of this class of hearts the organ presented the appearances commonly seen after death by asphyxia. It was also observed that the intestines were usually the seat of active peristaltic movements.

We could scarcely anticipate that the difference in the mode of introducing this poison into the system could so affect the after phenomena. It has, indeed, been noticed by others that convulsive motions are more common in animals poisoned by woorara when the poison is ingested than when it is inoculated, and this fact we have also verified; but that the action of the heart should be so differently affected by the two modes of administering the agent we have employed, was an unlooked for result. It certainly appears, from the experiments detailed as well as from others which are not stated, that when vao is inoculated it checks the heart's action, and even in some cases annihilates its sensibility to direct stimulation, before the nerves and voluntary muscles have ceased to obey volition. On the other hand, when vao is absorbed from a cutaneous or a mucous surface, the phenomena march more slowly, and the frog is left a lifeless mass, to all appearance, his nerves deprived of responsive irritability, and his voluntary muscles only alive to the direct action of galvanic currents, while the heart is still beating, or is at least awake to the galvanic stimulus.

The mode in which the heart is arrested is worthy of note. In cold-blooded animals poisoned by vao there is no primary stimulation of the heart. It beats progressively more slowly, until the ventricle acts only in parts of its bulk, and finally ceases to move. Next the auricles stop, the right pausing first. The manner in which the tissue of the heart behaves under the influence of corroval has been already described very fully. In fact, nothing can be more curious than the bulging out of the fibers of the ventricle in places. The same phenomenon occurs in poisoning by vao, though far less marked.

In this poison, as in the corroval, this arrest of the heart's movement is due to paralysis of the muscular fibers of the organ. This paralysis appears to be localized at first in spots here and there in the ventricle, and afterward to become general. To it are due, we conceive, the curious projection of small portions of the ventricle when the poison is fully affecting the heart. That this is the cause of the phenomenon in question may be made clear by tying the aorta of a frog, when the same phenomena present themselves as the organ becomes paralyzed from the distention to which it is exposed. A very interesting demonstration of the cause of the local prominences which we have described as marking the action of these poisons on the central organ of circulation, may be obtained by galvanizing portions of the ventricle in a frog which has taken no vao. Wherever the current passes, there is seen at the next contraction of the ventricle a prominent red elevation. The galvanism seems to over-stimulate, and thus paralyze a portion of the tissue. The rest of the heart contracts as usual, and the weakened galvanized portion is filled full of blood, and puffed out above the level of the active surrounding tissues.*

* The phenomena here described are among the most curious and striking physiological facts which have come under our consideration. The appearance presented by the heart, either where vao or corroval has been used, or when alternating galvanic currents have affected its tissue, is not easily described, so as to give any clear idea of the extraordinary behavior of the organ under these circumstances. When the current affects the whole ventricle, it becomes large, and ceases to beat. When a small portion of the ventricle is included in the circuit, this alone pauses, and at the next beat of the ventricle makes a hernia-like projection from the neighboring tissues. The prominences so formed are of a deep-red tint. At the next action of the heart they are less marked, and in each succeeding ventricular contraction they are less and less distinct, until only a slight flush marks the spot, and this also finally disappears. To prove conclusively that these effects are due to an over-stimulation, and a consequent temporary paralysis of the affected part, it is only requisite to over-stimulate, by mechanical means, a portion of the muscular fibers of the ventricle, when the same results occur to a more or less marked extent.

Now whether the paralysis of the heart is due to a direct effect upon its muscular tissues, or to a paralysis of the ganglia of the heart, is a question which can scarcely be solved without a previous determination of the exact cause of the heart's rhythmical action. Since, however, the muscles of the heart so soon cease to be galvanically irritable after they have ceased to move automatically, and since it can be shown that the muscles elsewhere lose irritability earlier than usual, it is probably a direct effect on the muscular fiber of the heart which causes its arrest. If, in fact, the loss of motion were due to a nerve paralysis, the muscular tissue ought to be long afterward responsive to stimulus. Whereas this is not the case in corroval poisoning, and only so in vao poisoning to a less extent than is usual in cold-blooded animals. Judging from warm-blooded animals only, we should conclude that vao killed by asphyxiating the animal, and thus arresting the heart. Whereas it is most probable that it is the early enfeeblement of the circulation which gives rise to a co-ordinate arrest of those muscular and nervous functions which are essential to produce and sustain respiration.

We have, however, a better proof at hand to aid us in showing that the checked respiration is only a last link in the chain of causes which produce death. The frog will live for many hours without breathing otherwise than by the skin; yet if a frog be poisoned with vao, he dies, the heart being arrested, and certainly without asphyxia having taken place. Again, in the poisoned alligator, respiration by the lungs goes on quite actively some time after the heart has ceased to move.

Respiration.—In cold-blooded animals, as the frog, and where the poison acts rapidly, the respiratory motions of the jaw, and sometimes of the flank, not unfrequently continue after the heart's movements are at an end, but the efforts thus made do not fill the lung. When the frog is poisoned through the skin or mucous surfaces, the action of the heart long survives the respiratory motions.

The fact of the continuance of efforts to breathe after the heart has entirely stopped, has been already alluded to. In the various experiments upon the effect of vao on the other functions, will be found such record of the fact as renders it unnecessary to repeat here the statements of experiments already quoted.

Calorification.—We have not thought it requisite to examine the effect of corroval upon the temperature of animals poisoned by it, because it acts with so much rapidity that it is scarcely possible the animal could lose enough of heat to be appreciable, before the heart stopped. For similar reasons M. Bernard did not find any change of temperature in the animals poisoned with ordinary woorara.

In the volume so often quoted, he records a single experiment upon the temperature of animals killed by woorara, and seems to entertain no doubt as to the generality of the conclusion stated in that connection. He found that in warm-blooded animals the temperature did not fall before death. Not having a specimen of the woorara used in Europe, we are unable to verify this observation, which is doubtless correct as regards that variety of poison. In fact, it slays with such rapidity, and with so little primary effect upon the circulation, that a fall of temperature is scarcely to be anticipated where the dose is large and the death sudden. Whether any other result would occur if the amount given were so small as to insure a more lingering death, we are unable to say.

In animals poisoned by vao, the period of time which elapses between the administration of the poison and the entire cessation of movement in all the muscles except that of the heart is so considerable that the failure of the respiratory acts is gradual. In such cases, therefore, the death is at least in part, if not wholly, a death by asphyxia, as we have already shown; and hence a fall in temperature is naturally to be expected. The following experiments are sufficiently definite as to this point:—

Experiment. A gray rabbit received in the thigh a morsel of vao, at thirteen minutes after five.

Normal temperature of the rectum $101\frac{1}{2}^{\circ}$ F. At the close of twenty-three minutes he began to chew, as though eating, gritting his teeth at intervals. His head fell forward now and then, as though he were drowsy, and was jerked up again with a quick movement, only to sink lower a moment afterward. In twenty-eight minutes he fell on his right side, the heart beating more slowly. The eyelids next grew insensible to a touch, the pupils dilated, and slight convulsive motions of the ears and hind legs took place. Temperature of rectum, $97\frac{1}{2}^{\circ}$ F. It continued to fall up to 6 P.M., when it was no longer observed. The heart was still acting at this time, beating about once in the minute.

Experiment. A large and very vigorous rabbit was selected, and a thermometer oiled and introduced into the rectum, where the temperature stood at 104° F. Fifteen drops of a solution of vao in water, 3 grs. to ℥j , were then injected into the areolar tissues of the thigh, when the following series of observations were made :—

Time.	Rectal temp.	No. of respirations.	
7-20	104		
7-25	$103\frac{3}{4}$	104.	The temperature with which the experiment began was unusually high for the rabbit, whose normal heat is from 101° to $102\frac{1}{2}^{\circ}$, or even 103° F. The rabbit had, however, struggled very violently, and hence, in all likelihood, the very elevated temperature first noted, and the consequent depression when he became entirely tranquil.
7-30	103°	128	
7-40	$102\frac{3}{4}^{\circ}$		
7-43	$102\frac{1}{2}$	128.	Struggles.
7-45	$102\frac{1}{2}$	96.	Head drooping.
7-47	$102\frac{1}{4}$		
7-50	102	100	
7-52	102	96	
7-53	$101\frac{3}{4}$	80	
7-55	$101\frac{1}{2}$	72.	Slight convulsion; eyelid irritable; pupil large; general movement of the skin muscles.

Time.	Rectal temp.	
7.57	101 $\frac{1}{4}$.	Irregular and rare.
7.58	101.	Respiration ceased; the skin muscles were still moving quite actively; the head fell; the pupils dilated; the eyelid no longer irritable; the heart still beat feebly; at

Time.	Temperature.	
8	100 $\frac{3}{4}$	
8.4	100 $\frac{1}{4}$.	Pupil contracting.

At 8.8 he was opened, when the heart was found to be yet beating well though feebly. The heart was very irritable to mechanical stimulus. The muscles elsewhere responded to galvanism, but not at all to mechanical irritation. Up to 9 the temperature continued to fall, when the observation terminated.

Experiment. A healthy pigeon, scantily fed, had at 1.56 P.M. a rectal temperature of 106° F., a morsel of vao being placed under the skin of his thigh. The following record of temperature was obtained:—

Time.	Temperature.	
1.56	106°	
1.58	105	
2.1	104 $\frac{1}{2}$	
2.2	104 $\frac{1}{4}$	
2.4	104	
2.6	103 $\frac{1}{4}$	
2.8	103.	When his head drooped and fell; the eye closed, and respiration stopped.
2.14	102	
2.17	101	
2.21	100	
2.25	99	
2.29	98.	No rise of temperature was observed up to 3 P.M., when he was no longer observed.

It follows very plainly from these, and similar results which we do not think it requisite to quote, that the temperature of warm-blooded animals poisoned by vao falls considerably before death occurs.

The Nervous and Muscular Systems.—The effect of vao upon the irritability of the nerves and of the voluntary muscles is best considered together, since, in the experiments upon this point, the condition of the nerves and muscles was recorded at the same time.

In this connection, it became necessary to determine—1st. Whether the nervous irritability lasted as long as that of the voluntary muscles. 2d. Whether the poison affected the motor or sensory nerves first, or whether both were equally attacked at one and the same time. 3d. Whether, as in the poisoning by ordinary woorara, the irritability of the muscles remains for a greater length of time than it does after death by decapitation or otherwise.

Experiment. A large frog received under the dorsal skin a morsel of vao. In forty minutes all volitional control had departed. The left sciatic nerve was then isolated, divided, and the ends put upon a piece of glass. When the central end was galvanized, slight twitches occurred in the other leg, showing that the power to carry impressions to the centers, *i.e.* sensibility, was not extinct. On galvanizing the distal end of the nerve, the muscles to which it is distributed contracted freely. Twenty minutes later both extremities of the nerve refused to obey the galvanic irritation, although the muscles were still excitable by direct irritation.

Experiment. Four hours after a morsel of vao was placed under the skin of a frog he was motionless, and no reflex motions could be obtained, except in the eyelids. At this time the left sciatic nerve was cut across. Galvanic irritation of the digital end had no effect on the muscles, which, however, continued irritable, when directly galvanized, during seventeen and a half hours.

Experiment. A frog was poisoned like the one last described. His heart ceased beating in thirty minutes, when the nerves were

still irritable. Their vitality, however, rapidly diminished, and was gone in two hours, the muscles remaining alive to galvanic irritants during fourteen hours only.

Experiment. A frog received in his back a small piece of vao. In forty minutes the voluntary motions were lost, and feeble reflex actions could still be provoked by pinching the legs. The eye was still irritable. At this moment the right sciatic nerve was isolated and divided without causing muscular motions in the leg. On galvanizing the centrally connected end of the nerve, one slight movement took place in the other leg. Irritation of the digital end of the nerve produced slight twitches in the peroneal muscles. Thirty minutes later both ends of the nerve were no longer irritable. The heart and muscles were still contractile when galvanized, but not when mechanically stimulated. The left leg and the rest of the body of the frog were then carefully protected by damp cloths; a dead frog being laid upon the leg on which we had operated in order to guard it from the direct effects of the moisture. In despite of these precautions, the nervous and muscular irritability was totally extinct at the close of forty-eight hours.

Experiment. A large frog received in the peritoneal cavity one drachm of the weak solution of vao, one grain to one ounce, his right femoral artery having been previously tied so as to prevent the poison from having access to the tissues of this limb. The right leg now moved with more difficulty than the left. One hour and twenty minutes after the poisoning both sciatic nerves were divided. On galvanizing them both, the muscles of the leg whose artery was tied moved freely; the nerve of the uninjured leg being galvanized, feeble motions occurred in the muscles. Half an hour later the nerve of the uninjured side lost the power to evolve movement in the muscles, while galvanic irritation of the leg whose artery was tied gave rise to free motion in its muscles. The part which was protected from the poison by

having its artery tied, therefore retained the irritability of its motor nerves longer than the part which was exposed to the poison. On dividing the spinal column, half an hour later, in this frog, and thrusting a probe upward, the eyes alone moved; when the probe was thrust downward, no motion resulted.

Experiment. A large frog received in his back, under the skin, fifteen drops of a solution of vao, of the strength of five grains to one ounce of distilled water. At the close of three hours, the nerves of the leg were cut across and galvanized at the digital end, causing some movement in the muscles of the calf and foot. The muscular irritability was already enfeebled. An hour later the motor nerves had lost all irritability, while the muscles were so much enfeebled that they responded but slightly when directly galvanized. The muscles of the under jaw remained irritable longer than any others, and this is usually the case in poisoning by vao.

It becomes sufficiently clear from the foregoing experiments that, under the influence of vao, the irritability of the motor nerves in the frog is lost very early, and that the irritability of the muscles is also enfeebled and finally destroyed much sooner than is usual.

It is also clear that in frogs which are poisoned rapidly by a large dose of vao, the nerves of motion cease to functionate before the muscles are deprived of the power to respond to direct stimulus—another proof, if any were needed, of the independence of the muscular irritability, and of its absolute want of connection with that of the nerves.

To make the matter more perfectly clear and definite, a number of comparative experiments were made.

Experiment. A frog was poisoned with the vapor of ammonia. At the end of twenty-four hours none of his muscles were irritable. They were not examined earlier than this.

Experiment. A frog killed with atropine retained his muscular

irritability during twenty-seven hours and thirty minutes, when the observation terminated.

Experiment. Of two frogs killed by decapitation, the museles remained irritable in one during thirty-nine, and in the other during forty-eight hours.

Like results were obtained in all cases of death by decapitation. Now it is well worthy of remark that on comparing our own researches upon this special point with those of the French observers, it is seen that the normal irritability of the museles is less persistent in our frogs than in those used by the *savans* in question. In many instances stated by Bernard and others, the muscular irritability of decapitated frogs lasted during five or six days, whereas in no case has it remained in our own frogs after fifty hours. The temperature is one of the most important factors in this very interesting problem. In warm weather the irritability departs very early, and unfortunately M. Bernard does not state the condition of the thermometer at the time he made his experiments. Our own researches were conducted in a room whose temperature ranged during the period of our examinations from 49° to 68° F.

The determination of the fact of the early loss of muscular irritability under the use of vao, separates it widely from ordinary woorara, which, according to M. Bernard, not only does not weaken the museles, but actually prolongs very remarkably the period during which they may be made to respond to galvanic or other stimuli.

In no instance was it found that vao affected the movement of the cilia in the frog's throat.

Having thus determined that the functions of the nerves are destroyed before those of the museles succumb, and also that the muscular irritability is weakened and finally annihilated long before the time when the same result is observed in many other modes of death, we have yet to consider the remaining questions

as to the order of abolition of function in the two great classes of nerves, motor and sensor, and as to the influence of vao upon the brain and the sympathetic system.

The woorara of European observers, according to M. Bernard, acts first upon the motor or efferent nerves, and destroys all reflex acts very early, because the efferent nerve which is first paralyzed is essential to the production of these phenomena. A frog which has taken woorara is, therefore, physiologically in the same state as one which has had the motor roots of the spinal nerves cut across. To test this with vao poison—

Experiment. A large frog was selected, and a ligature tied around the right femoral artery. The voluntary actions ceased very early. The legs were sensitive to direct galvanic stimulus. Slight reflex movements occurred in the legs, and the eyelids winked when touched. When the belly or back was galvanized, the leg in which the artery was tied responded by reflex movements. The other leg did not stir. On isolating its nerve and galvanizing the distal end, its muscles moved, though feebly. The nerve of the other leg being similarly irritated, vivacious motions took place in its muscles. The poison had gone too far and acted too rapidly to make this a satisfactory experiment. It showed doubtfully that both orders of nerves were affected to some extent, and it also indicated the greater tenacity of life in the upper part of the body, where the eyelids continued irritable and where the muscles under the jaw responded when the motor manifestations were weak in all other parts of the body exposed to the action of the vao. At the close of an hour and a half the spine was destroyed, when the leg which had been operated upon moved slightly. No other motion resulted, and the muscular irritability was extinct in five hours.

Experiment. A large frog poisoned by vao was motionless in three hours, save that the eyelids still acted. His left femoral artery had been previously tied. The right sciatic nerve was ex-

posed, divided, and the two ends insulated on glass. As the poison had been cut off from the left leg, it could not share in any supposed loss of motor power, should such exist. If motion was lost in the poisoned parts and sensation remained, an irritant applied to the centric end of a nerve in the poisoned part would convey the stimulant effect to the nerve centers of the spine, and the nerve of the unaffected limb ought to acknowledge the irritation by reflex acts. The irritation of the poisoned nerve would be felt by the nerve centers, but in case the motor functions of the poisoned parts were abolished, no muscular reflex act could result anywhere, save in the unpoisoned limb, whose nerve and muscles would, so to speak, translate into the language of motion the reflected impression. Such does occur with ordinary woorara. In the present instance neither the galvanization of the fore legs nor of the centric end of the right sciatic caused motion in the unpoisoned leg, which, however, moved vivaciously when directly stimulated. A probe thrust down the spine produced free motion in the leg the artery of which was tied, and some twitches in the other. The defect of reflex motion was, therefore, not due to want of life in the motor nerves or the spinal centers.

Experiment. The sciatic nerve of the left hind leg of a frog was isolated, and a wire being passed beneath, it was carried around the rest of the limb and tightly twisted. Vao was then employed as usual. The right brachial nerve was galvanized after the reflex motions had become extinct to all appearance; slight movements took place in the leg of the same side, but no form of stimulus applied to either brachial nerve caused motion in the leg on which we had operated. The twitches above mentioned showed, however, that both motor and sensory power was feebly preserved even in the poisoned parts. A little later no such motions could be had, although the poisoned limbs still moved for a time when their nerves were directly stimulated.

Experiment. A very large frog had his sacrum removed, so as

to expose the lumbar nervous plexus. A ligature was cast about the rest of the body, excluding these nerve-trunks. As the ligature arrested the circulation, the bridge of nerves alone connected vitally the two segments of the frog. A solution of vao was now injected under the skin of the trunk, above the ligature. Two hours later, the reflex acts being at an end in the upper parts of the frog, the brachial nerves were irritated, but without evolving the slightest motion in the unpoisoned limbs. Direct stimulus applied to the lumbar plexus caused free movement in the legs.

In the next experiment the brain was removed before the frog was poisoned. His reflex motions were well developed, but faded rapidly. The nerves of the arms were galvanized, and by degrees lost the power to provoke motion elsewhere; while, at the same time, their muscles still moved when the distal end of the nerve was galvanized.

Experiment. A large frog was chosen, and the heart exposed. A large amount—twenty drops—of a solution of vao, five grains to the ounce, was put under the skin of the back. In fifteen minutes the ventricle stopped, and the auricles also ceased beating in twenty-five minutes. Three hours after the poisoning one sciatic nerve was uncovered and galvanized by a powerful alternating current; the muscles of the same leg responded freely. The nerve was then cut, and the centric end galvanized, without any reflex acts occurring. The lumbar nerves were next tested, but still with no result as to reflex motion elsewhere. Finally an examination of the nerves of the other limbs showed that their nerves still retained motor power, and that their muscles were sufficiently irritable.

It becomes very clear from these experiments, and others which we cannot afford space to quote, that vao acts first upon the sensitive nerves, and not, like other woorara, upon the motor filaments. Its next action is upon the motor function of the nerve-trunks, and lastly upon the independent irritability of the muscles.

In almost all of the experiments, although the fore legs were first affected in the paralysis which finally involved all parts, the respiratory muscles under the jaw and the muscles of the eyelids remained active long after all the rest, although so feeble that their efforts did not suffice to fill the lungs.

It has been shown conclusively, in the early portions of this paper, that the mere stoppage of the circulation by ligation of the vessels at the base of the heart produced a rapid and complete loss of nervous but not of muscular irritability. The paralysis of the nervous system, under the use of vao, is therefore due, in all probability, to the enfeeblement and final loss of cardiac power. The defect of muscular irritability must be a result of the poison acting on the tissue of the muscles themselves.

Effect of Vao on the Blood.—After repeated examinations of the blood of animals killed by this poison, we have been unable to trace the slightest alteration in the form of the blood globule when the perfectly fresh blood was inspected. If it be allowed to stand some time, either within the animal or after removal from its vessels, the usual alterations in the form of the disks may be seen. One observer, at least, has conceived that ordinary woorara affected the forms of the blood disks; but all subsequent investigations have been opposed to this view, and it is probable that his examination of the vital fluid was delayed so long as to permit of those changes in form through osmosis to which the delicate red corpuscles are so familiarly liable.

We have also studied the blood with reference to the influence of vao on its coagulation, and on its power to absorb oxygen. Neither in frogs, in rabbits, nor in birds has vao appeared to retard the coagulation of the blood. In one single case, that of a cat, this act was unusually delayed.

In the frog and the alligator the lung appears to supply sufficient red blood up to the last moment to redden the heart in

one-half of its area until the ventricle ceases to move. Where, therefore, asphyxia is not an essential result, as in these cold-blooded animals, the heart is checked by the vao before any marked change has taken place in the color of the blood. In warm-blooded animals—cats, rabbits, mice, birds, etc.—the final link in the chain of causes which produces death is asphyxia from want of muscular movement. Here the blood is black, and the heart presents the appearances commonly observed in asphyxiated animals. The power of this dark blood to reabsorb oxygen was ascertained in the following manner: The blood of a large rabbit, poisoned with vao, was whipped as it escaped into a vessel, to free it from fibrin. Thus prepared, it was agitated in a bottle with atmospheric air, when it was soon observed to have recovered its bright arterial hue.

Before we call attention to the subject of the differences between corroval, woorara, and vao, it has occurred to us that it would be as well to state the physiological evidence bearing upon the question of what it is that gives the deadly potency to corroval and vao. A portion of such evidence is to be found in the chemical and microscopical characters of these poisons, and we shall in this place insist alone upon certain interesting physiological facts. The old opinion as to the activity of woorara being due to the venom of poisonous serpents is still to some extent a popular belief. To examine this matter anew, with reference to the poisons before us:—

Experiment. A large frog was chosen, and a small scale of dried venom from the rattlesnake was placed under the skin of the back. This poisonous material is nearly two years old, and is in the form of dry yellow scales upon the side of a bottle. It was obtained by one of the authors of this paper—Dr. Hammond—by holding a snake with its upper jaw over the edge of the bottle, so that, on irritation, the poison was discharged into the interior of the bottle.

During twenty-five minutes the frog, poisoned as described, was unusually active. At the close of this period it became more quiet, and occasional twitches were observed in the hind legs, which were also extended spasmodically at intervals. Ten minutes later it lay quiet as placed, in any position, breathing at intervals. The eyelids were irritable, and reflex motions could be provoked. All voluntary power seemed to have fled. One hour and ten minutes later the reflex motions still occurred when irritants were used, and the twitching and extension of the legs continued. It was now becoming rapidly enfeebled. Two hours and fifty minutes after the administration of the poison no motions could be evolved, and it was then laid open. On applying the galvanic current to the voluntary muscles no motion occurred, and the nerves were of course unable to produce any muscular response when galvanized. The heart was still beating.

A second experiment, of a similar nature, was made upon a large frog, with nearly similar results, except that death did not occur until five hours after the venom was used. It was noted in this case, as a curious fact, that the eyelids were insensible before the reflex movements of the extremities were lost. After all reflex motion had departed, the heart, which was large and almost black, continued to act during more than two hours in all of its cavities. During this time the nerves and muscles were more or less irritable when galvanized. The vitality of both nerves and muscles was lost within five hours after the heart had ceased to act.

These two cases differ from one another in certain particulars which demand the future criticism of experiment; but at present it is enough to point out the dark and swollen state of the heart, its long-continued and perfect action in all its parts, and the occurrence in both frogs of local spasms of the muscles, as well as occasional convulsive extensions of the hind legs, as marking a

difference between the venom and both corroval and vao, which we hope to examine more fully at another time.

It might naturally be supposed that the local character of the wounds would also constitute a further ground of distinction. We were not astonished, however, to observe that the rattlesnake poison produced no local effect in the frog. The wound in which was placed vao, corroval, or the dried venom of the *Crotalus confluentus* was not in any way to be distinguished by the eye. Meanwhile, it is to be observed that the animals used were cold-blooded reptiles, which are not capable of developing inflammatory action, such as is observed in the tissues of mammals similarly treated.

Again, it is worthy of note that the venom employed was two years old, and perfectly dry. How far this may have modified the result we are as yet unable to say. A pigeon, poisoned with the dried venom of the crotalus, died in two hours and fifty-two minutes. Two minutes after the wound was made in its thigh it had become black. Around this a ring of a deep amber color was seen, and before death a dark serous fluid exuded from the wound. A simple wound made at the same time exhibited no such phenomena. Very little swelling occurred about the poisoned wound, and no general swelling of the body was observed. Soon after the inoculation was effected the pigeon rocked on its feet, staggered, fell, and rose again, flapping its wings, and vomiting corn from the crop. A half hour later it gradually sank down, the breathing grew labored and uneasy, and the heart beat rapidly. The temperature fell to 94° F. one hour and thirty-two minutes after the poisoning, and continued to fall, until, when it reached 88° F., death occurred, during general but not very violent convulsions. Rigor mortis came on within forty-two hours. On examination of the blood globules, they presented no unusual or abnormal peculiarities. The local affection is in this warm-blooded bird the distinctive difference between the action of vao

or corroval and that of the serpent poison. In both cases asphyxia is in warm-blooded animals the last link in the chain of causes which produce death.

It is, then, highly improbable that the venom of serpents is used in the manufacture of the poisons before us. As it is stated that ordinary woorara is formed from the juice of the *Strychnos toxifera*, and as the alliances of this plant would seem to make it probable that it contained strychnia, it became interesting to know whether that substance might not have been so altered by the long boiling required to prepare the woorara as to change its character and affect its toxicological peculiarities. Accordingly a grain of strychnia was boiled with gum starch and water for nine hours, without in the least impairing its peculiar qualities. A frog poisoned with the mixture died, tetanized as usual. We desired to ascertain, in the next place, whether, if our own vao poison contained strychnia, it would be so modified by the other constituents of the poison as to lose its peculiar powers. A minute portion of strychnia was therefore added to a little vao, and the two poisons inserted under the skin of a frog. He perished in tetanic spasms, and the heart stopped soon after death. The same effects were observed when corroval and strychnia were separately introduced under the skin in two distinct localities. Now as the heart of the strychnized frog will beat for some hours after all externally visible motion has ceased, it is plain that in the double poisoning both agents produced their own distinct and peculiar effects. The one caused tetanic spasms, the other paralyzed the heart. It is therefore sufficiently clear that no form or modification of strychnia is present in the vao or corroval.

In addition to the negative evidence here adduced, we have the more positive results which have been stated in connection with the physical and chemical examination of the two poisons. From the whole evidence, we feel authorized in considering both poisons as of vegetable origin.

The history of the antidotes to this poison may be very shortly summed up.

Sir Walter Raleigh, in his very curious account of the arrow-poison, tells us that the Spaniards were cured of ordinary poisoned wounds by the use of the juice of the garlike, (garlic,) in which, however, he reposes but little faith. His own remedy, a knowledge of which he professed to have obtained from the Indians, he thus describes: "But this is a general rule for all men that shall hereafter travell the Indies, where poisoned arrows are used, that they must abstain from drinke, for if they take any licor into their body, as they shall be marvellously provoked thereunto by drought. I say if they drink before the wound be dressed, or soone upon it, there is no way with them but present death."* The next allusion to antidotes is equally vague, and it is even doubtful whether the poison alluded to has any analogy to the woorara at present known, since it is said by the authority referred to, that it kills only after seven days. De la Vega further informs us that to arrive at a knowledge of the antidote, the Spaniards wounded an Indian with a poisoned arrow, and then setting him free, observed that he chose certain herbs, which he ate, and applied locally, with entire success.†

De la Condamine‡ is the first writer who speaks of sugar and salt as antidotes. After returning to Cayenne, he made a few experiments with woorara, thirteen months old. Of two chickens which were poisoned by woorara, and treated with sugar internally, one died. Afterward, at Leyden, and before Mussenbreck, Van Swieten, and Albinus, the sugar antidote totally failed. Some of De la Condamine's woorara passed into the hands of

* Sir W. Raleigh. Disc. of Guiana, p. 71.

† The Royal Commentaries of Peru. By the Inca Garcilasso de la Vega. London, 1688, p. 741.

‡ Tr. de l'Acad. des Sci., 1745, vol. lxii. p. 489.

M. Hérissant,* who used sugar and wine as antidotes in the case of a lad who had been left to watch some of the poison which was boiling in a small and close room. The boy became weak, and was supposed to have been a sufferer from the poisonous fumes. It is needless to add that in his case the sugar acted perfectly. Not so fortunate were ten birds, which were poisoned by M. Hérissant with a mixture of Lamas and Ticunas, and instantly fed upon sugar. Nine of them perished. Salt proved equally unsuccessful, whereas instant amputation, or the actual cautery, saved the life of the animal. A single experiment was made as to the value of the ligature as a safeguard. Although applied to the limb beforehand, it failed entirely. M. Hérissant also essayed the effect of large bleedings, after the poison had been given to horses. Of six so treated, two recovered.

Schomburgk,† whose work is of comparatively recent date, repeats the old story of sugar and salt as antidotes, adding that the whites alone repose confidence in their protecting power. The Indians, who are said to place but little reliance upon any of the supposed antidotes, mention, as the best, cane-juice (sugar) alone, or mixed with an infusion of the root of the wallabo, (eperua or dimorpha.)

Bancroft‡ relates that "the white inhabitants of Guiana consider sugar, *i.e.* cane-juice, as a remedy in poisoning by the acawau, a variety of woorara. The Indians themselves do not acknowledge this property of the cane; and," he adds, "I have never been able, either by my own experiments or inquiries, to discover a single instance of its efficacy for that purpose."

With Fontana§ began the closer examinations of this singular poison, which have made its modern physiological history a matter of such deep interest. This observer found that when the

* Phil. Trans., vol. xlvii. p. 75. 1746.

† Schomburgk, 1847.

‡ Bancroft, p. 297.

§ Fontana, vol. xi. p. 118. 1781.

mineral acids were mingled with the Ticunas poison, it was rendered innocuous as an injection under the skin, or as a local application upon the bare muscles. The same result ensued when the acids were evaporated with the poison, and the residue was employed. Neither vinegar nor rum were of any avail as antidotes, when mixed with the Ticunas.

Osculati* also alludes to the antidotes, and states that a mixture of salt and sugar acts as such when taken freely, but that it is also essential to place in the wound a weapon dipped in this mixture, and to continue taking the not very agreeable compound of dissolved salt and sugar for some time afterward. This statement is mere hearsay, and rests upon no experiments by the author of the paper in question.

The experiments of Drs. Brainard and Green, first in Chicago, and afterward in Paris,† lead these gentlemen to consider the mixture of iodide of potassium and iodine as an antidote, when mingled with the poison in solution. These experiments are quoted and commented upon by Dr. Green himself, in a paper on woorara, which he has written since the date of the communication to the academy, of his own results, and those of Dr. Brainard.‡ The last-named researches shortly afterward elicited from M. Reynoso an admirable paper§ upon the use of various agents as antidotes to woorara. In reviewing the essay of Drs. Brainard and Green, he classes as a caustic the iodine solutions employed by these gentlemen. He therefore attempted to render the iodine harmless to the tissues, while securing its primitive action upon the woorara. Having found that iodide of potassium used alone with woorara solution did not prevent, but

* Osculati, p. 201. 1850.

† Comptes Rendus de l'Acad., vol. xxxviii. p. 411. 1854.

‡ Am. Med. Gaz., vol. vii. Nos. 5 and 7; vol. vii. No. 1. 1845-6.

§ Reynoso, Comptes Rendus de l'Acad., vol. xxxix. p. 68. 1854.

merely delayed its ultimate manifestations, he made the following experiments :—

Half a gramme of iodide of potassium and 0·4 gramme of iodine, with 0·06 gramme of curare in solution were treated with hyposulphite of soda, drop by drop, until the iodine disappeared, when the mixture was rendered alkaline by the addition of carbonate of soda. This mixture killed in twenty minutes, when injected under the skin. A mixture of alcohol, iodine, and curare did not prove fatal; but when, in such a mixture, the iodine was rendered inactive, by the use of the hyposulphite of soda, poisoning followed its use, in one hour and forty minutes. M. Reynoso thence concludes that iodine alters the poison, but does not destroy it. Hypochlorite of lime also delayed the action of the woorara. Experiments were further instituted, which seem to show that chlorine in a nascent or free state destroys the poison. Chloride of sodium mingled with it did not save the animals tested with this mixture.

In another series of experiments, the author added 10 gtt. of bromine to 0·06 gramme woorara, and 7 cubic centimetres of water. This mixture was rendered fully alkaline by carbonate of soda, and some few drops of hyposulphite of soda were added. It was injected into the subcuticular tissues of an animal, who died in twenty-four hours, in collapse, poisoned by the bromide of sodium, which, used alone, was found to be fatal in a like dose. When a mixture of woorara and bromine was heated until the bromine escaped, the residue was harmless when injected into animal tissues.

Sulphuric and nitric acids, caustic potash, lime-water, and ammonia-water all retarded the action of woorara when mixed with it. Certain salts which are not caustic, such as the iodide and bromide of sodium, and iodide of potassium, also exercise a retarding influence; but this effect M. Reynoso looks upon as undoubtedly local, since iodide of potassium, given internally, does

not prevent the poison from proving active when afterward used subcutaneously. Doctors Brainard and Green, and M. Reynoso are of opinion that the application of the cupping-glass, so long as it is kept applied, prevents the poison from being absorbed.

Notwithstanding the ingenuity of M. Reynoso's experiments, they do not entirely settle the question of antidotes to woorara, and while the action of certain salts in delaying the absorption, or the after-action of the poison, is distinctly made out, we are still left in the dark as to the cause of this effect from the use of an agent so harmless as iodide of potassium. Even upon M. Reynoso's showing, the solution of iodized iodide of potassium used by the American experimenters would have the double advantage of a cauterizing and a delaying agency when used with the poison or put instantly upon the wound.

With woorara, as in many other kinds of poisoning, artificial respiration, maintained for a length of time, saved the animal, when the dose of the poison was not overwhelming. Waterton's experiments on this subject are very striking, and are the last to which we shall refer, since the very recent writers, as Kölliker and Bernard, have merely quoted their facts from M. Reynoso's paper, which we have already analyzed. It is unnecessary to quote here the simple experiments which satisfied us that neither sugar nor salt has any claims to be regarded as an antidote. Since, however, Brodie, Waterton, and others had previously found that by sustaining artificial respiration time was allowed for the elimination of the woorara, and the animal escaped death, we resorted to the same expedient in rabbits and cats poisoned by corroval and vao. In no instance was the death even so much as retarded, and the heart ceased to beat as soon as usual. This result could have been anticipated, from the fact that in the alligator thus poisoned, respiration continued perfect long after all cardiac movement had departed. In one sense, therefore, corroval and

vao are more deadly agents of destruction than common woorara, since, for them, no physiological antidote of any kind exists, while in poisoning by woorara, at least one resource is available.

Conclusions.—1. Vao, either in a solid, or more quickly in a liquid form, can be absorbed from the areolar tissues of cold-blooded animals, as the frog.

2. It is also absorbed by the stomach, œsophageal mucous membrane, rectum, and skin, with a degree of rapidity which varies, and is rapid or slow as the animal is ill or well supplied with water.

3. Warm-blooded animals absorb vao from the stomach and intestine when they are fasting, but suffer no ill effects when the vao is given during digestion. That this protection is not due to a mere mixture of the vao with the food of the full stomach, is shown by the fact that rabbits, whose stomachs are always more or less distended with food, are protected only when, owing to the entry of fresh food, digestion becomes active.

4. The demands of the system for water do not affect to any perceptible extent the absorption of vao from the stomach of the rabbit.

5. The circulation of the frog is arrested within from ten minutes to one hour by the introduction of vao under the skin. The same result obtains within from twenty-four to forty-eight hours, when the poison is swallowed in small doses.

6. The first effect of vao is to increase the force of the heart without increasing the number of its pulsations.

The next effect is a paralysis of the muscular tissues of the heart, so that the ventricle stops first and the right and left auricles next, in the order in which they are named. In a majority of the frogs poisoned by vao, the heart remained galvanically irritable for a certain time after the organ had ceased to pulsate.

The heart stops before the voluntary motions are at an end, in all cases of rapid poisoning. When poisoning occurs by absorp-

tion from a mucous surface, the phenomena march more slowly, and voluntary control and reflex power are sometimes lost before the heart has entirely ceased to beat.

7. Vao stops the respiration in warm-blooded animals by arresting the circulation, and so paralyzing the nervous system, without which respiration is impossible; so that the checked respiration is a consequence and not a cause of the injury to the cardiac functions.

In the batrachia, also, the respiratory movements cease before the heart has entirely lost the power to pulsate.

In the alligator poisoned by vao the respiration is perfect some time after the heart is at rest.

8. The facts last quoted, and the inability of artificial respiration to restore or sustain the cardiac movements in warm-blooded animals poisoned by vao, prove sufficiently that the first effect of the poison is upon the heart, and that the appearances of asphyxia observed *post mortem* in rabbits, cats, etc. are of secondary importance so far as concerns the cause of death.

9. The temperature of warm-blooded animals poisoned by vao falls with considerable rapidity, and does not undergo any elevation after death.

10. The nerves of sensation first lose their power to convey impressions—the motor nerves are next affected. The paralysis of the nerves extends from the periphery to the center. The affection of the nervous system may be due to the sudden arrest of the circulation, and not of necessity to the direct influence of the vao. The irritability of the voluntary muscles in the frog is lost much earlier than is the case when the animal dies by decapitation.

11. The sympathetic nerve is paralyzed, at least in the upper portion of its distribution, before the nerves elsewhere have lost their functional power.

12. The ciliary motion is unaffected by the use of vao.

13. The blood of animals thus poisoned coagulated as usual, and had not lost the power of changing color when exposed to oxygen or carbonic acid.

14. So far as we are aware, no true physiological antidote exists for vao poison, since even artificial respiration fails to sustain life in animals affected by it.

15. The vao poison closely resembles corroval in its physical, chemical, and physiological reactions. The alkaloids extracted from the two poisons produce in animals of equal size effects which cannot be distinguished from each other.

We, therefore, are inclined to consider vao as merely a weaker variety of corroval, and to conclude that the apparent difference in the effects produced by the original extracts is due to a difference in their strength.

We have thus brought to a close an investigation which has involved considerable labor, and we now submit our results for the consideration of the profession. No statement has been made in this essay, and no conclusion deduced, of the accuracy or truth of which we at least are not fully satisfied. How far this may be the case with others we cannot say; and, at all events, whatever be the fate of these researches, we shall at least have had the pleasure of the pursuit, and the satisfaction of stimulating inquiry upon questions of interest and importance. With the words of the venerable Abbé Fontana, whose labors in the field of biological investigation have been too much neglected, we would say, in conclusion, "Those only who observe and experiment, make mistakes; those only who do neither, never err."

ON THE

PHYSICAL AND CHEMICAL CHARACTERISTICS

OF

CORROVAL AND VAO

TWO RECENTLY DISCOVERED VARIETIES OF WOORARA,
AND ON A NEW ALKALOID CONSTITUTING
THEIR ACTIVE PRINCIPLE.*

THE two new varieties of woorara, which, so far as relates to their physical and chemical characteristics, we design considering at present, were brought in February, 1857, from the Rio Darien, in New Granada, by Drs. Ruschenberger and Caldwell of the United States Navy. By these gentlemen they were presented to Prof. Joseph Carson, of the University of Pennsylvania, to whom we must express our acknowledgments for the opportunity afforded us of analyzing and experimenting with these curious poisons.

The corroval, the more powerful of the two, has the general appearance of a vegetable extract of a brownish-black color. The fracture is somewhat conchoidal, but some of the fragments in our possession have a surface such as would be given to the superficies of an inspissated vegetable infusion on cooling. When pulverized, it is of a tawny yellow appearance. Its taste is an

* In conjunction with Dr. S. WEIR MITCHELL.

intense and very persistent bitter. The saturated aqueous infusion is of a very dark-brown, almost black color, and of neutral or exceedingly slight acid reaction. The alcoholic tincture is of a pale-yellow tint. Both water and alcohol extract the poisonous principle, as do also ether and chloroform, though to a very diminished extent. No crystals are deposited from any of these solutions, except from the ethereal. They consist entirely of fatty substances.

The residue, insoluble in water, submitted to microscopical examination, is seen to consist of vegetable cells, starch granules, portions of woody tissues, oil globules, etc.; small grains of silica are also to be observed. No parts of animals of any kind can be discovered by most careful examination with object-glasses of high power and excellent defining quality. If the fangs of poisonous serpents, the livers and other parts of the body were used in the manufacture of corroval, we should undoubtedly have detected their anatomical elements. We therefore regard it as certain that such substances do not enter into the composition of the material under consideration.

Corroval burns with a yellow flame, and gives off a considerable amount of smoke and vapor. This latter has an odor very similar to that of human excrement, and, as we have ascertained, possesses all the poisonous activity of the corroval in substance. A mouse made to inhale the fumes died in less than two minutes. Corroval heated upon platinum foil, in the flame of the blow-pipe, is almost entirely volatilized. The ash consists of silica, iron, and certain saline substances.

In external characteristics it cannot be distinguished from corroval. That in our possession is a dark-brown extract, hard, and perfectly dry, and unaffected by exposure to the atmosphere. It yields its toxic principle to water and alcohol, the infusions being of similar physical qualities and reaction with those of corroval. The insoluble portion consists of a white or light gray

deposit of a shred-like and flocculent appearance. Examined under the microscope, this is seen to be principally composed of amorphous matter, with which, however, starch granules and cells of vegetable origin, together with masses of woody tissue and fragments of silica, are mingled. No animal structures are to be detected on the most minute examination.

Vao subjected to the action of heat acts in a manner not distinguishable from that of corroval, giving off a vapor with similar odor, and other properties to that derived from the latter substance.

Woorara, of which corroval and vao may with propriety be considered as constituting species, has been analyzed by Roulin and Boussingault,* Pelletier and Petroz,† and Heintz.‡

Roulin and Boussingault experimented with woorara which had been obtained from the Rio Negro. It was a solid extract of a black color, but brown when reduced to powder, of a resinous appearance, and exceedingly bitter taste. It burned with difficulty, and gave off no odor of organic nitrogenous substances. It was soluble in water, alcohol, and in sulphuric ether, though not to any considerable extent. The aqueous infusion was of slight acid reaction; no strychnine was discovered by these chemists in woorara.

We may here state that two specimens of ordinary woorara, which we owe to the kindness of Major Le Conte, of Philadelphia, and Prof. J. C. Dalton, of New York, agree in all essential particulars with that above described.

By the following process, Roulin and Boussingault obtained

* Examen Chimique du Curare, Poison des Indiens de l'Orinoque, Annales de Chimie et de Physique, tome xxxix., 1828, p. 24.

† Examen Chimique de Curare, Annales de Chimie et de Physique, tome xl., 1829, p. 213.

‡ Reisen in Britisch Guiana, von Richard Schomburgk, Band i. S. 452, (note.)

from woorara a new principle of an alkaloidal character, which they called curarin.

The woorara was reduced to fine powder and treated repeatedly with boiling alcohol. The extract thus obtained was evaporated, and the solid residue treated with water, which dissolved the active principle, leaving nothing but a little resinous matter. The aqueous solution was then decolorized by animal charcoal, and treated with infusion of galls. A beautiful whitish-yellow, flaky precipitate was then thrown down, having an exceedingly bitter taste. The supernatant liquid was almost entirely deprived of its bitterness; the precipitate thus obtained was well washed, heated to ebullition in water, and dissolved by the addition of oxalic acid. The acid liquor was then supersaturated by magnesia, and filtered. It was again evaporated to dryness, and the residue dissolved in alcohol. This solution was concentrated and spontaneously evaporated to a syrupy consistence. It was subsequently further concentrated by evaporation *in vacuo*.

The analysis of Pelletier and Petroz yielded a similar product. These chemists extracted the woorara with alcohol, and treated the tincture thus obtained with ether, in order to remove the fatty and resinous substances present. The alcoholic extract was then evaporated, dissolved in water, and foreign matters precipitated from the solution by the acetate of lead, the excess of lead being removed by sulphuretted hydrogen. The solution was then decolorized by animal charcoal, filtered and evaporated; sulphuric acid diluted with absolute alcohol was then added, for the purpose of draining off the acetic acid. The alcohol was removed by evaporation, and the sulphuric acid precipitated by baryta. The excess of the latter was separated by carbonic acid, the liquid was next filtered and concentrated in the water-bath, and the curarin thus obtained further dried *in vacuo*.

Obtained by either of these processes, curarin is a solid, transparent, resinoid substance, of a pale-yellow color, very hygro-

scopic, and soluble to almost any extent in water and alcohol. Its taste is exceedingly bitter. The solution in water restores the blue color to reddened litmus paper, neutralizes acids, and forms salts with them, easily soluble in water, but uncrystallizable.

Curarin gives, with concentrated nitric acid, a blood-red color, and, with concentrated sulphuric acid, a carmine tint.

Heintz proceeded as follows: To the aqueous solution of the woorara tannic acid was added, and an abundant precipitate soluble in boiling water was obtained. This was taken from the filter, boiled with magnesia, and then evaporated to dryness. The extract thus obtained was then treated with alcohol, to remove it from any insoluble salts of magnesia, and the solution again evaporated to dryness. By this means a yellowish-brown extract was obtained, possessing no alkaline reaction, but endowed in an eminent degree with the toxic principle of the woorara. Heintz does not regard this extract as at all pure; subsequently he employed both the bichlorides of mercury and platinum to effect the precipitation, but with no better success, a yellowish extract being still obtained.

Heintz ascertained by Lassaigne's method that the extract contained nitrogen; he also found sugar, gum, resin, extractive matter, and tannic and gallic acids; traces of saline combinations with organic acids, probably the tartaric and oxalic, were also detected. He was unable to discern the least trace of strychnia.

We think it highly probable that the woorara examined by Heintz was very far from being of identical character with that analyzed by Roulin and Boussingault and Pelletier and Petroz. The difference in the process employed is not sufficient to account for the very dissimilar product obtained by Heintz. His method was certainly such as to have separated any alkaloidal principle present. The substance he did obtain was probably

nothing but a purified and more highly concentrated woorara, deprived of its woody fiber, starch, silica, etc.

We now proceed to detail the several steps in a qualitative analysis made of the corroval and vao.

A few grains of corroval were subjected to the action of ether. From the solution thus obtained, oil globules were deposited, on evaporation, together with a number of minute acicular crystals, insoluble in water but completely dissolved by hot alcohol and ether. Globular masses of a supposed resin were also present.

To another portion, water was added till it was completely extracted of all its bitter principle. The residuc was perceived to contain several masses apparently of a fatty character. On subjecting this substance to the action of hot ether, it was entirely dissolved, and on evaporating the solution from a slip of glass, and viewing the residue with the microscope, numerous delicate acicular crystals collected in groups and radiating from a central nucleus were perceived. These were soluble in hot alcohol. The remaining portion was in the form of oil-globules.

After thus separating the fatty substances as above, the portion insoluble in water was placed in a small retort with a little water; a receiver surrounded with ice was luted to the retort, and heat applied to the latter. On the surface of the distillate a small portion of essential oil floated. This had an odor somewhat resembling that of mustard, but much less pungent.

The substance remaining in the retort was next dried at a low temperature, and subjected to the action of alcohol. A yellowish-brown solution resulted, from which, on evaporation, a resinoid substance was obtained, having an odor very similar to that of a true essential oil.

The residue was next calcined in a platinum crucible. By this process the woody fiber, etc. was consumed, hydrochloric acid was added to the ash, and the silica thus separated. To a portion of this solution in hydrochloric acid diluted with water, ferro-

cyanide of potassium was added, and distinct evidence of the presence of iron obtained. Another portion treated with bichloride of platinum gave, after a lapse of several hours, a reddish crystalline precipitate, indicating the presence of soda.

We were prevented, by an accident, from continuing the analysis of the above portion.

The aqueous solution was found, by the addition of gelatin in excess, to yield a flaky, yellowish-white precipitate of tannate of gelatin. It was filtered, and to the filtrate perchloride of iron added. A black precipitate of gallate of iron was thrown down.

From the foregoing analysis we conceive that we have ascertained the existence in corroval, besides the active principle, of the following substances: Olein, margarin, essential oil, resin, starch, silica, iron, soda, woody fiber, tannic acid, and gallic acid.

The small quantity of corroval in our possession prevented us from extending our analysis further in this direction, and for the same reason we are the less disposed to insist upon the absolute accuracy in all its steps of the foregoing investigation. Several of the above-named substances were detected by the microscope alone, and this instrument was constantly employed throughout the whole analysis.

In the separation of the active principle of the corroval, we made use of the following processes:—

1st. Ten grains of the substance were extracted by repeated portions of boiling water, till a bitter taste was no longer afforded. The solutions were now mixed and boiled with magnesia. It was next filtered, and the filtrate filtered repeatedly through animal charcoal, till all the bitterness and coloring matter were entirely absorbed. The charcoal was then treated with boiling alcohol, in fresh portions, till all bitterness was extracted from it. The alcohol was then evaporated to dryness. By this means a very bitter substance of a greenish-white color was ob-

tained, possessed in a high degree of the toxic properties of the corroval.

2d. The process employed in this instance was that first used by Roulin and Boussingault, but modified by employing water to extract with instead of alcohol.

Ten grains of the corroval were reduced to fine powder and extracted with water, as in the first described process. To the solution, tannic acid was added in excess; a voluminous flaky precipitate of a yellowish-white color was thrown down. This was well washed on a filter to remove the tannic acid, mixed with water and heated to boiling, a few crystals of oxalic acid being added till it was entirely dissolved. The acid liquor was next treated with magnesia in excess, and filtered. The filtrate was evaporated to dryness, and the extract thus obtained dissolved in hot alcohol. This solution, evaporated to dryness, furnished a substance similar to that obtained by the first process, but more highly colored.

For the principle thus obtained, possessing as it does the properties of an alkaloid, and in a high degree the toxic properties of the corroval, we propose, in accordance with the principles of the United States Pharmacopœia, the name of *corrovalia*.

Corrovalia* is, when pure, a greenish-white substance, of low specific gravity, and, upon the whole, similar to tannic acid in general appearance. It is soluble in alcohol, ether, and chloroform, and, contrary to the statement in our original memoir, to a slight extent in water. Heated upon platinum foil, in the flame of a spirit-lamp, it is entirely volatilized. With concentrated nitric acid it gives an emerald-green color, which deepens in tint if a small piece of bichlorate of potassa be added. With sulphuric acid, a reddish-brown color is formed, which, with the

* Experimental researches relative to Corroval and Vao, etc., American Journal of the Medical Sciences, No. lxxv. N. S., July, 1859.

further addition of bichromate of potassa, changes in a few minutes to a deep olive green; with ammonia it gives a deep yellow color, but no precipitate; with potassa in solution, the result is much the same; with tannic acid, it gave a white precipitate.

With iodide of potassium in solution, corrovalia yielded no precipitate or change of tint, nor did it give rise to any reaction in the presence of bichloride of platinum.

Corrovalia is uncrystallizable from all its solutions, except from that in chloroform. A drop of the chloroformic solution evaporated to dryness on a slip of glass, and subjected to microscopic examination, exhibits numerous acicular crystals, mostly collected in groups and radiating from common centers.

Corrovalia neutralizes the sulphuric, chlorohydric, and acetic acids, and in all probability others, the quantity in our possession being too small for us to investigate its properties further in this direction. The salts formed with the above-mentioned acids, as far as we have been able to ascertain, are uncrystallizable.

Introduced into the blood, corrovalia exerts a toxic power equalled by few if any substances hitherto known to man. A grain was dissolved in one hundred minims of water. One minim of this solution killed a small mouse in five minutes, when inserted under the skin, and five minims in four and a half minutes produced the same result in a medium-sized rabbit. With frogs it is especially active.

The amount of alkaloid obtained by us from corroval, amounted to about ten per cent.; from vao, the proportion did not exceed four or five per cent.

Vao is, therefore, much weaker than corroval; its physiological action is very similar to the latter substance. The amount of resin contained in it is considerably greater than that found in the corroval, as is also the woody fiber. For the physiological effects produced by these new and curious poisons, we must refer to the memoir to which we have already alluded.

Owing to the small quantity of these substances in our possession, we have been unable to make an ultimate analysis of them, and consequently cannot at present give formulas of their composition. In other respects we have from the same cause been unable to carry our investigations as far as we desired. We, therefore, hesitated to publish the results of our examination of the chemical nature of these poisons, but upon more mature reflection have concluded to lay them before the scientific world, trusting at some future period to be enabled to present a more complete memoir on the subject, and to correct any errors into which we may have fallen in the course of the researches just concluded.*

* Proceedings Acad. Nat. Sci. of Phila. Biological Dep. April, 1860. Some misconception appears to have been occasioned by the names under which we have studied these poisons. In our first essay they were distinguished as "Corroval and Vao, two new varieties of woorara, the South American arrow-poison." In consequence of this title, it has been supposed that we regarded corroval and vao as identical with the woorara of De la Condamine, Köl liker, and others. No person, however, who went beyond the title of the papers, could possibly entertain this idea, since the toxicological distinction is drawn in the most definite manner. All the specimens of corroval and vao which we have seen have come to us labelled *woorara*, and we have been informed that this term, or the more specific appellation, were indiscriminately used by the Indians of the Rio Darien.

EXPERIMENTAL RESEARCHES

RELATIVE TO A

SUPPOSED NEW SPECIES OF UPAS.

Among the most deadly poisons which the ingenuity of man has devised for purposes of destruction, must be placed the two well-known species of upas employed by the natives of the Indian Archipelago. While woorara, corroval, and vao are used by the aborigines of a portion of the western continent as death-dealing agents, the Javan possesses poisonous compounds scarcely, if at all, inferior in virulence to those mentioned, and around which, for a long period, hung as much mystery as was ever attached to their American analogues.

In bringing to notice in the present memoir, what, for several reasons, (which will hereafter be made apparent,) I am disposed to regard as a new variety of upas, it may not be uninteresting or unprofitable to recapitulate briefly the progress and present state of our knowledge relative to the history, chemistry, and physiology of the species of East India arrow-poisons hitherto described.

An arrow-poison in use among the natives of Macassar is mentioned by Sir Thomas Herbert,* whose work is the earliest on the subject to which I have been able to refer According to

* Relation of some Yeares Travaille. London, 1634, p. 199.

Bennett,* it is mentioned by De Bry,† in a work published some years previously to that of Herbert.

Herport‡ and Saar§ are also quoted by Bennett, as having written upon the subject in the years 1669 and 1672, and as stating that human ordure, taken internally, is an antidote to the effects of the poison in question. That some such idea as this was prevalent in Europe at the time, we are led to believe from the fact that the following question formed one of several on the subject, proposed by the Royal Society,|| for Suratte and other parts of the East Indies: "Whether it be true that the onely antidote hitherto knowne against the famous and fatal Macassar poison, is humane ordure taken inwardly, and what substance this poison is made of?"

Tavernier¶ also mentions this poison; speaking of the inhabitants of Macassar, he says:—

"These islanders are in the habit of poisoning their arms, and the most dangerous poison they employ is the juice of certain trees which grow on the island of Borneo, which they modify according to the effect, either rapid or slow, which they desire to produce. It is said that the king alone knows the secret of lessening the activity of this substance, and that he boasts of possessing some poison so powerful that there is no antidote in the world to its virulence. One of my brothers, whom I had taken with me to the Indies, and who died there, was witness of a remarkable proof of the promptitude with which this poison produces its effects. An Englishman having, in the heat of passion, killed one of the subjects of the king of Macassar, and the prince

* Horsfield's *Plantæ Javanicæ Rariores*, p. 53.

† *India Orientalis*, Pars 8, p. 81.

‡ Kurtze Oest Indianische Reise Beschreibung, 1669, p. 26.

§ Oest Indianische Funfzehn Jahrigr Kriegsdienste, pp. 46, 47.

|| *Philosophical Transactions*, vol. i., 1666, p. 417.

¶ *Les six Voyages de Jean Baptiste Tavernier*, etc. Paris, 1676, seconde partie, p. 438.

having pardoned him, all the French, English, Dutch, and Portuguese, who were then at Macassar, fearing that if the murderer remained unpunished, the natives would be revenged on them, prayed the king to inflict death upon the Englishman, to which he at length consented. The death of the Englishman having been agreed upon, the king said to my brother that he would not let him languish, and that, to demonstrate at the same time the extraordinary strength of his poison, he would himself shoot the prisoner with one of his arrows. These are little poisoned arrows which are shot from a blow-gun, and the king, to show at the same time his skill, asked my brother in what part of the body he wished him to shoot the criminal. My brother, who was very desirous of ascertaining whether that which the king had said relative to the prompt action of the poison were true or not, desired him to shoot the prisoner in the great toe of his right foot, which the king did with wonderful address. Two surgeons, one English and the other Dutch, were present to cut off the toe above the wound, but they could not do it so quickly but that the poison more prompt had reached the heart, and the Englishman died at the same time.* All the kings and princes of the east seek with great care for the strongest poisons, and the king of Achen one day made Mr. Cook, Envoy of the General of Batavia, a present of fifteen or twenty of these poisoned arrows. He had possessed them for some years without making trial of them; but being one day with him, he shot several squirrels with them, all of which fell dead as soon as struck."

Cleyer† furnishes some information on the subject, which he

* The similarity of the incidents of the above relation, with those told by Fermin as occurring with the woorara of Guiana, is so striking, as to lead to the supposition that this writer derived the materials of his account from Tavernier's story.

† *De Telis deleteriis venenâ infectis in Macassar et aliis Regnis Insulæ Celebes, etc.*, *Miscellanea Curiosa Academiæ Naturæ Curiosum*. Norimbergæ, 1699. *Decuriæ* ii. Ann. ter. 1684, p. 127, et seq.

obtained from the diary of Cornelius Spielman, Commander of the Dutch East India possessions.

According to this writer, there is no antidote to the poison used by the natives of Macassar, if it be recent. He, however, states the best remedy to be human excrement taken internally till vomiting be produced.* He also states that the land in the vicinity of the trees from which the poison is derived is entirely barren, and that no plant of any kind is able to grow on it. The collectors of the poison use long bamboo rods with sharp points for the purpose of piercing the trees, and thus obtaining it without bringing it in contact with their bodies. The poison hardens in the canes, and is subsequently softened with water, in which an herb called *lampogang* has been infused.

Gervaise* asserts that the poisoned arrows retain their activity for twenty years, but that exposing them to smoke destroys their toxic power. He also declares that the action of these arrows is so rapid that death ensues immediately, and before any antidotes can be employed.

Among the plants sent from Luzoni by Father Kamel,† was a specimen of the tree from which the poison in question was asserted to be prepared. According to the description given, the ipo or hypo is of medium size, with small leaves, and of so virulent a character that every living being coming under its shade dies, and that hence for some distance around each tree the bones of men and animals are found. The assertion of previous authors is repeated relative to the efficacy of human excrement as an antidote.

Rumphius‡ gives a long description of the tree, accompanied by several figures, together with a detailed account of the poison, its action, etc. He describes the tree under the name of *arbor*

* Description Historique du Royaume de Macassar. Paris, 1688, p. 45.

† Ray's Historia Plantarum, London, 1704, tome iii. Appendix, p. 87.

‡ Herbarium Amboinense, tome ii. liber iii. p. 263.

toxicaria ipo, giving the name upas as a synonym. This tree, he asserts, grows in Celebes, Sumatra, Borneo, and Bali. Most of the information he furnishes in regard to it and its poison was obtained from the natives, and, as is usual in such cases, is distorted by statements wholly devoid of truth.

Foersch,* in the latter part of the eighteenth century, gave circulation to the grossest falsehoods relative to the upas. Many authorities might be quoted, whose chief object seems to have been the denial of Foersch's statements, and the institution of others fully as questionable. I shall, however, pass them all over, and at once refer to writers whose accounts possess more truth than fiction.

The first writer who investigated the subject in a truly scientific spirit, was M. Leschenault.† Up to his researches, the two species of upas had not been distinguished, either by origin or by their effects, when introduced into the circulation of animals. A chemical analysis had not even been thought of. Leschenault showed conclusively that two species of poison, differing essentially in composition and effects, were used by the natives of the Eastern Archipelago. With these they charge little arrows of bamboo, which are shot from blow-guns. The flesh of animals killed with these arrows possesses no injurious quality, it being only necessary to remove the parts in immediate contact with the poison. One of these poisons is called upas antiar, the other upas tieute. This last is more violent in its action, and is less known, as the Indians make a secret of its preparation, which is more complicated than that of the upas antiar.

According to Leschenault, the upas tieute is prepared in the following manner: The bark of the root of a creeper, called by the natives tieuté, is boiled in water till a saturated infusion is

* London Magazine, December, 1783, p. 511.

† Mémoire sur le strychnos tieute et l'antiaris toxicaria. Annales du Museum d'Histoire Naturelle, tome xvi., 1810, p. 459.

obtained. This is reduced, by continued evaporation, to the consistence of a thick syrup. When this point is attained, two onions, a clove of garlie, a large pinch of pepper, two small pieces of the root of the *Kæmpheria gallenga*, three small pieces of ginger, and a single grain of *capsicum fruticosum* are added. This mixture being made, it is left for a short time longer on the fire and allowed to become clear. Three pounds of bark give about four ounces of extract. Leschenault charged two arrows with it, and after allowing them to become dry, pricked two chickens with them. One died in about a minute in violent convulsions, the other in a similar manner at the end of two minutes. Other animals were also killed with it; and MM. Delille and Magendie found that it had not lost its power at the end of four years. These experimenters also ascertained that the upas tieute acts through the blood-vessels and absorbents upon the spinal cord, causing tetanus, asphyxia, and death.

The upas antiar, according to the same author, is prepared with the gum-resin which flows from the trunk of a very large tree, from incisions made for the purpose. The poison is made in an earthen vessel, without the aid of heat. To the gum-resin are added a few grains of capsicum, some pepper, garlic, and the roots of *Kæmpheria gallenga*, *maranta malaccensis*, and *costus arabicus*. Each one of these substances is bruised and gradually added, with the exception of the grains of capsicum, which are one by one rapidly thrust to the bottom of the vessel by means of a little wooden spit. Each grain occasions a slight action in the liquid, and rises to the surface. It is then withdrawn and others added, to the number of eight or ten, when the preparation is finished.*

* I am indebted to my friend, Dr. Joseph Carson, Professor of Materia Medica in the University of Pennsylvania, for the following botanical description of the plants yielding the two species of upas:—

“*Strychnos tieute*, Leschenault. *Gen. Char.*—Calix 45 parted; corolla

The effects of the upas antiar are not so violent as those produced by the upas tieute, and Leschenault has clearly pointed out the difference. A small water-fowl which he inoculated with it died in three minutes, having had no convulsion till the instant of expiration, whereas with the upas tieute strong tetanic con-

tubular, with a spreading 4-5 cleft limb and a valvate æstivation; stamens 4-5, inserted into the throat of the corolla, which is either naked or bearded. Ovary 2-celled, with indefinite ovules attached to a central placenta; style 1; stigma capitate. Berry corticated, 1-celled, many-seeded, or by abortion 1-seeded; seeds nidulant, discoidal; albumen large, cartilaginous, almost divided into two plates; embryo with leafy cotyledons.—Lindley.

“Specif. Char.”—A large climbing shrub, with a thick woody root, 1-2 inches in diameter, and extending far under ground horizontally. Stem as much as 80-120 feet long, twining itself around the loftiest trees. The branches diverge at the extremity of the ramifications, and are opposite on the stem, being twisted and leafy. The leaves are opposite, oval, lanceolate, 3-nerved, entire, acuminate, and glabrous. Hooks solitary opposite the leaves, thickest at the points; cymes oscillary, lax; corolla $\frac{3}{4}$ ths of an inch long, funnel-shaped, greenish-white, with the smell of jasmine. Fruit the size of a middling apple, each placed on a short thick flexicose peduncle, which is thickest at the point, globose, smooth, shining, at first brownish-yellow, afterward bright pink.

“Antiaris toxicaria—Leschenault. This plant was placed by Lindley, in his *Flora Medica*, in the family uricacæ; its alliances have subsequently appeared such as to warrant its removal to artocarpacæ, a family which, singularly enough, alongside of this venomous plant, embraces the edible bread-fruit. Its poisonous qualities still are allied to those of several species pertaining to the first-named order.

“Gen. Char.”—Monœcious; male flowers on a convex fleshy receptacle, scaly on the under side, and there attached by a stalk in the middle. Sepals 3-4, imbricated. Anthers 3-4, nearly sessile. Female flowers solitary, on a scaly peduncle. Calix none. Ovary 1-celled; ovule inverted; style 2-parted. Fruit a fleshy 1-seeded drupe. Embryo inverted, without albumen.—Lindley, *Flora Medica*.

“Spec. Char.”—A large-sized tree, with a trunk marked by prominent excrescences. The leaves are alternate, oval, oblong, and either obtuse or pointed, unequally caudate, coriaceous, when young toothletted, petiolate and hairy. The male flowers are united in a common hemispherical, pedunculated, and axillary fungus-like receptacle. They are green, downy, and separated by numerous imbricated scales. Female flowers are solitary, and almost sessile at the axilla of the leaves. Numerous imbricate scales cover the ovary, which is surmounted by two stigmata.”

vulsions were always produced. Magendie and Delille also demonstrated, by the difference in their physiological effects, the non-identity of the two poisons.

Brodie's* experiments with the upas antiar are of great interest. He found that when introduced into the circulation of animals, vomiting ensued, the heart beat feebly and irregularly, and there was great languor. Respiration, however, was perfect, and the cerebral functions were not disturbed. On opening the thorax before respiration had failed, the heart was found to have ceased contracting, and was gorged with blood. From his investigations he concludes that :—

“The upas antiar, when introduced into a wound, produces death by rendering the heart insensible to the stimulus of the blood, and stopping the circulation. The heart beats feebly and irregularly before either the functions of the mind or the respiration appear to be affected. Respiration is performed even after the circulation has ceased, and the left side of the heart is found after death to contain scarlet blood, which never can be the case when the cause of death is the cessation of the functions of the brain or lungs.”

Horsfield† has given a full account of these poisons, and performed many experiments with them. His account of the methods used in the manufacture of the antiar and tieute does not differ essentially from Leschenault's relation, and need not therefore be further considered. Horsfield performed two series of experiments; the first, with the antiar, were instituted upon numerous mammals and birds. The symptoms observed were, in general, vomiting, convulsions, evacuation of feces, and death in periods varying from a few minutes to several hours. The experiments of the second series were performed with the tieute upon mammals

* Philosophical Transactions, Part I., 1811, p. 198.

† Thomson's Annals of Philosophy, vol. ix., 1817, pp. 202, 265.

and birds. This poison was found to be much more virulent than the antiar. It produced convulsive twitchings, rigidity of the muscles, great exhaustion, and death. From post-mortem examinations, he concluded that the action of the antiar is directed to the viscera of the thorax and abdomen, and that of the tieute to the brain and dura mater.

It cannot be said that Horsfield's experiments are such as to throw much light upon the physiological action of these substances. He, however, gives some interesting details relative to the plants from which they are obtained. From these it appears that the antiar or anchar is one of the largest trees of the Archipelago, rising to the height of sixty or eighty feet before sending off a branch. It proves hurtful to no plant around it, and creepers and parasitical plants wind around it in great profusion. The poison is situated in the bark, from which, when cut, it flows in the form of a milky sap. In this state it is as deleterious as when mixed with extraneous substances, as black pepper, ginger, etc. When applied to the skin, it produces intolerable pain and itching, with a kind of herpetic eruption.

The tieute chetik or tschetic, according to the same author, is only found in Java.

Blume* states that the antiaris toxicaria grows not only in Java, but also in the neighboring islands, and in most of the groups of the Indian Ocean. By the inhabitants it is called ipo, hypo, or upas, words which in the different Malay dialects signify poison, and which are also applied to the strychnos tieute or bohon upas, (poison tree.) In Java it is specially designated by the names antchar, antzchar, or antjar.

Blume also states that the poison is of a volatile nature, and that the deleterious principle is lost unless it is carefully preserved from contact with the atmosphere.

* Rumphia, tome i. p. 36, et seq. See also tab. 22 and 23.

According to the same author, the antiar does not act with equal promptness on all animals—dogs, for example, being less affected by it than monkeys, cats, or bats. Certain birds die almost at the instant of inoculation, while chickens are but slightly affected. It is less active when introduced into the stomach than when injected directly into the circulation, and in the former case induces vomiting. It is further asserted that emetics are the best antidote.

The chemical examination of the tieute and the antiar instituted by MM. Pelletier and Caventou,* gave results of considerable importance. From the investigations of these chemists it is conclusively shown that the active principle of the upas tieute is strychnia united to an acid, probably the igasuric, while the upas antiar contains a bitter matter soluble in alcohol and in water, and possessing the same toxical properties (though in much greater degree) as the antiar in substance. To this principle the name of *antiarin* is given.

Mulder† has also analyzed the antiar. A specimen brought to him from Java, by Blume, he found to possess the following constitution :—

Vegetable albumen	16·14
Gum.....	12·34
Resin.....	20·93
Myricin.....	7·02
Antiarin.....	3·56
Sugar.....	6·31
Extractive.....	33·70

Antiarin can be obtained by boiling the upas antiar in alcohol. On cooling, the antiarin crystallizes in silvery inodorous leaflets of mother-of-pearl luster, which are soluble in 250 parts water,

* Examen Chimique des Upas, Annales de Chimie et de Physique, tome xxvi. p 44.

† Traité de Chimie de Berzelius, tome iii. p. 869.

70 parts alcohol, and in 2792 parts ether, melt at 220 C., and are not volatile.

No investigations of any importance were instituted subsequently to the foregoing with either species of upas, till a short time since Prof. Kölliker* communicated the results of some initiatory researches relative to the physiological action of the upas antiar.

The specimens of the poison employed by Kölliker were obtained from Drs. Christison and Horsfield, and originally came from Borneo and Java. That from the latter locality, though collected in the beginning of the present century, was found to possess its full toxical power.

The symptoms which followed the introduction of the antiar into the circulation of frogs were as follows:—

In the first place, the voluntary movements became less energetic, and at length entirely ceased, in an average period of from 30 to 40 minutes after the inoculation. Reflex movements could be excited for a short time subsequently, but they were soon lost, (in from 50 to 60 minutes from the commencement,) and the animals died without the least trace of convulsion or tetanic spasm. Upon opening the frogs it was invariably found that the heart had ceased to beat. The auricles were dilated; the ventricle contracted, corrugated, and generally red, as if blood had been extravasated into its tissue. The other organs, especially the lungs, liver, stomach, intestines, and kidneys, were found in a hyperæmic condition. The excitability of the nerves was still present, but in slight degree, and was generally abolished in the second hour after the introduction of the poison. The irritability of the muscles to galvanism was lost a short time after that

* Einige Bemerkungen über die Wirkung des Upas Antiar, Verhandlungen der Würzburgener Phys. Med. Gesellschaft, Band viii., 1857. See also Proceedings of the Royal Society, December, 1857.

of the nerves. The *rigor mortis* commenced in the sixth hour and was generally well established at the eighteenth hour.

It was definitely ascertained from these experiments that the heart of frogs inoculated with antiar ceases to beat in from five to ten minutes, and that the ventricle ceases acting before the auricles. The first action of the antiar is therefore to paralyze the heart. By further investigation, Kölliker ascertained that the abolition of voluntary and reflex movements was entirely due to the stoppage of the heart's action, for by cutting out the heart or putting a ligature around the base of it, as had been previously done by other observers, it was found that the voluntary movements ceased in from thirty to sixty minutes, and the reflex actions in from one to two hours. The irritability of the nerves and muscles was not thus abolished, consequently the antiar exercised a direct action on these organs.

From a third series of experiments, Kölliker arrived at the conclusion that the voluntary muscles are paralyzed next after the heart, and the nervous trunks some time subsequently. The antiar, therefore, unlike the ordinary woorara, acts principally upon the muscular system, and in confirmation of this conclusion, it was found that the muscles and heart of frogs poisoned with this latter substance lost their irritability in a short time if antiar was introduced into a wound some time after the woorara.

As the results of his researches, Kölliker deduces the following conclusions:—

- "1. The antiar is a paralyzing poison.
- "2. It paralyzes in the first instance the heart, acting with great rapidity upon this organ.
- "3. The speedy disappearance of voluntary and reflex movements is a direct consequence of the paralysis of the heart, at least the same results ensue upon extirpation or ligature of this organ.

"4. The antiar in the second instance paralyzes the voluntary muscles.

"5. In the third place, it subsequently paralyzes the great nervous trunks.

"6. In frogs poisoned with woorara the antiar exerts its peculiar effect upon the heart and voluntary muscles.

"7. From the foregoing it would appear that the antiar is principally a poison to the muscles."*

The researches of Pelikan,† relative to the action of the antiar, tend to the same general conclusions as those of Kölliker, and from the investigations of this observer it would appear that the alcoholic extract of the leaves and stalks of the *Tanghinia venenifera* produces analogous results—the main fact derived from his experiments being that both these poisons act directly upon the heart, arresting the action of this organ, but causing no tetanic spasms.

From the various examinations heretofore instituted, it would appear, therefore, to be definitely settled that the upas tiente causes tetanoid convulsions, but does not act primarily upon the heart, its action being in many respects similar to that of strychnia, which substance enters into its composition, while the upas antiar, like corroval, vao, and tanghinia, causes death by directly arresting the motions of the heart, but inducing no tetanic convulsions. The following investigations will show how very complicated is the action of the upas in my possession, and how essentially it differs from any other poison hitherto described.

* The great similarity existing between the action of the antiar, as above described by Kölliker, and that of corroval and vao, is very striking. See the paper on these latter poisons, in conjunction with Dr. S. Weir Mitchell, of Philadelphia, entitled "Experimental Researches relative to Corroval and Vao, two new varieties of Woorara, the South American Arrow-Poison." At the time these investigations were made we had not seen Prof. Kölliker's observations on the antiar.

† Beiträge zur gerichtlichen Medizin, etc., 1858, pp. 164–169.

The upas used in the ensuing experiments was obtained in 1848, by Dr. W. S. W. Ruschenberger, of the United States Navy, at Singapore. He knows nothing of its history before it came into his possession. I must express my sincere appreciation of his kindness in placing it at my disposal.

When the poison in question was given to me it was contained in a small phial, tightly corked and sealed, which had not been opened since it was procured. The contents were of semifluid consistence, of a dirty-green color with a slight yellowish tinge, and evolved a very decided odor of human feces. A slight sediment which had been deposited consisted of amorphous organic matter, with a few vegetable cells and other structures of similar character.

Desirous, in the first place, of ascertaining its physiological effects upon the animal organism, I was unable, from the small quantity in my possession, to subject it to so thorough a chemical examination as I desired. My investigations in this latter direction were therefore limited to one point—the determination of the presence or absence of strychnia.

For this purpose I proceeded according to the method of M. Stas for the detection of the alkaloids.

Twenty grains of the poison were diluted with about a drachm of water. A few minims of alcohol and five minims of acetic acid were next added, and the mixture digested in the water-bath for an hour and a half, being frequently stirred. The mixture was then filtered, and the residue washed with dilute alcohol till all soluble matter was extracted. The liquid was then evaporated nearly to dryness in the water-bath, and the residue treated with boiling alcohol and filtered. The alcoholic solution was again evaporated, and the residue digested with a small quantity of distilled water. The solution was filtered, and potash added till the reaction became alkaline. The mixture was then shaken in a stoppered test-tube with twice its volume of rectified ether. The

ethereal solution was then decanted, and allowed to evaporate spontaneously.

In this manner 4.75 grains, equal to 23.75 per cent., of a substance possessing an intensely bitter taste, but uncrystallizable, were obtained. Tested with bichromate of potash and sulphuric acid, a deep-blue color was produced, but this was not succeeded by the characteristic play of colors which strychnia produces; and although less than the fourth of a grain caused violent tetanic spasms and death in a large frog, I suspected that the substance obtained was not pure strychnia. I therefore treated it with pure distilled water, and found that to a considerable extent it was soluble in this menstruum. Of 4 grains thus acted upon, the residue amounted to 2.87 grains. This was crystallizable, as strychnia, and exhibited with bichromate of potash and sulphuric acid the same reactions as this substance. It also caused tetanus and death in a frog, when inserted in very minute quantity under the skin. The aqueous solution last obtained was preserved. It will be again referred to when the physiological experiments are detailed.

My impression from the results of this examination, and from the few experiments performed, was that the poisonous substance was the upas tieute. The place whence it was obtained, and the fact that it contained strychnia, were, I thought, sufficient to establish its identity. The more thorough physiological examination instituted, which I now proceed to detail, convinced me of my error.

In order to facilitate the introduction of the poison into the circulation of animals, twenty grains were diluted with two fluid drachms of distilled water, a few drops of alcohol being added to insure against decomposition. This was the strength always employed, unless otherwise stated.

The more obvious effects of the poison are shown in the following experiments:—

Experiment. Ten drops of the diluted poison were inserted under the skin of a large cat. During the first two minutes no symptom worthy of note was observed. Then slight twitchings of the muscles of the back were perceived, and immediately afterward the animal vomited. At the end of four and a half minutes the cat fell, and was tetanically convulsed. Death ensued immediately, in the midst of violent and general tetanic spasms. Circumstances prevented me making any further examinations in this case, and it is only adduced as being among the first of the series of experiments, and as showing with what great power the poison acted.

Taking, however, into consideration the results of the chemical examination, and the extreme rapidity with which death followed the first convulsions in the experiment just cited, I was strongly of the opinion that some other cause than tetanus was active in producing the ultimate result. I therefore proceeded as follows:—

Experiment. Three drops of the poison were inserted under the skin of the back of a large frog, and the chest immediately laid open, in order to observe the action of the heart. At the time, this organ pulsated fifty times per minute, and with great regularity. After the fourth minute the movements became more irregular, the ventricle contracted to less than half its normal size, lost its deep color, and finally ceased to beat, five minutes after the inoculation. The auricles stopped beating a few seconds subsequently. The frog, however, was still possessed of a good deal of muscular vigor, and was able to leap several feet. The animal was placed under a bell-glass, and carefully observed. Seven minutes after the movements of the heart were arrested there were slight convulsive actions of the abdominal muscles, and in less than a minute afterward the frog was in violent tetanic spasms. These were excited by the least irritation. They continued for nearly half an hour with undiminished violence, and

then gradually ceased. Fifty-five minutes after the inoculation, the animal was dead to all excitation.

Experiment. Ten drops of the poison were introduced under the skin of a medium-sized cat. At the end of seven and a half minutes the animal had a slight spasm and vomited. In two minutes afterward it fell, with general tetanic convulsions, and expired. The chest was immediately opened, and the heart was found to have ceased acting.

These experiments were frequently repeated, and always with analogous results. They lead inevitably to the conclusion that the poison used, besides inducing tetanus, acts directly upon the heart. In fact, in frogs its first effect is to arrest the action of this organ, and it is not till some minutes have subsequently elapsed that the tetanus supervenes. It is probable that the same is the case in mammals, but, owing to the rapidity with which the poison acts in warm-blooded animals, it is difficult to arrive at a very definite conclusion on this point. The following experiment, which was several times repeated with like results, shows at any rate that the heart is affected before any spasms occur:—

Experiment. Fifteen drops of the poison were inserted into the thigh of a small dog. The chest was immediately opened, artificial respiration being kept up by means of the apparatus described in the memoir on Corroval and Vao. The action of the heart was not more than ordinarily disturbed till about four minutes had elapsed. Portions of the left ventricle then became paralyzed, and the pulsations of the organ became much slower. Up to this period no convulsions had occurred; but shortly after the appearance of the phenomena above referred to, a slight tetanic spasm of the whole body took place. In less than a minute subsequently—about six minutes after the inoculation—the heart suddenly stopped, simultaneously general tetanic convulsions occurred, and the animal was dead.

It may therefore be concluded that the poison referred to in this memoir, like the upas antiar, corroval, vao, and tanghin, acts primarily upon the heart, but, unlike these agents, acts also upon the spinal cord, causing tetanic convulsions. Its action would therefore appear to be a compound of that of the two known species of upas, and it might be supposed that the poison in my possession was a simple mixture of these substances. In order to discuss this point properly, it will be necessary to return to the chemical examination made.

It will be recollected that 20 grains of the poison yielded 4.75 grains of an exceedingly bitter substance, possessing, in some respects, the characteristics of strychnia, but yet differing very materially from it in several essential particulars, and that this matter was further separated into strychnia and a substance soluble in water.

The solution of this latter ingredient, on being carefully evaporated to dryness in the water-bath, left a light-yellow substance, extremely hygroscopic, and possessing a somewhat astringent and slightly bitter taste, the latter being probably due to traces of strychnia. It was slightly soluble in alcohol, and very much so in ether, differing therefore in these respects from antiarin. It was also readily dissolved by chloroform. It was altogether uncrystallizable, another point of difference from antiarin.

In physiological properties it appeared to resemble this latter substance. A small portion, not larger than the head of a pin, arrested the action of the heart of a large frog in about four minutes. A pigeon inoculated under the wing fell dead in two minutes. On opening the chest, the heart was found hard and rigid. In neither case was there the least appearance of tetanic or other convulsions.

The quantity of this substance becoming exhausted, I was unable to experiment further with it. The chemical properties were certainly not those of antiarin, and therefore the idea that the

poison to which this memoir relates is a mixture of the upas antiar and the upas tieute is not tenable.

We have already seen that the primary action of the poison under consideration is upon the heart, and that secondarily it acts upon the spinal cord, producing tetanus. That this last-mentioned result is not a consequence of the arrest of the heart's action will be admitted by all who are familiar with the consequences which follow ligature or removal of this organ in frogs. In such cases there are no convulsions, the animal dying from complete abolition of all nervous action. From numerous experiments which I have performed with reference to this point, I have satisfied myself that after placing a ligature around the large vessels at the base of the heart, or extirpating the organ, the voluntary movements entirely cease in from twenty to fifty minutes, and the reflex in from one to two hours. My experiments in this respect are therefore entirely in accordance with those of Kölliker already referred to.

In an elaborate memoir lately published by MM. Martin-Magron and Buisson, it is attempted to be shown that both woorara and strychnia cause tetanus, and act upon the nervous system without the agency of the circulation.* It would be easy to show the numerous fallacies into which these physiologists have fallen, but such is not at present my intention. That the poison now under notice does not act but through the medium of the blood, the following experiments abundantly show:—

Experiment. A ligature was placed around the base of the heart of a large frog at 1.45; at 1.47 the animal was inoculated in the left posterior extremity with five drops of the solution of upas; at 2.15 voluntary movements abolished; at 2.55 no reflex actions could be excited. Nervous and muscular irritability re-

* Action Comparée de l'Extrait de Noix Vomique et du Curare. Journal de Physiologie de M. Brown-Séquard, numéros vii. viii. ix. 1859-60.

mained four or five hours longer. At no time was there the least appearance of spasm of any kind, though the animal was carefully observed till 9 o'clock.

Experiment. The entire heart was cut out of a large frog at 4·15, and the blood allowed freely to escape; at 4·18 the animal was inoculated with the poison in the left posterior extremity; at 4·53 voluntary motions were abolished; and at 5·38 reflex movements could no longer be excited. The animal was carefully observed till 11 o'clock, but no convulsions of any kind occurred.

Even if such actions had supervened, I do not think they would have afforded any proof that the poison was not conveyed to the spinal cord through the medium of the blood, for, as is well known, the capillary circulation persists in frogs with more or less activity for some time after ligation or extirpation of the heart. I have ascertained that six hours subsequently to either of these operations a persistent current in one direction only is present in the capillaries of the web, and that oscillatory movements continue for several hours afterward. If, therefore, a poison be applied to the spinal cord, or its membranes, or even in its vicinity, it need excite no surprise if the peculiar effects of the agent are manifested. I have frequently repeated the chief experiments of MM. Martin-Magron and Buisson, and though I have generally obtained their results, I think a different interpretation of them is required. At the same time I am not prepared to deny that poisons may act by imbibition in the manner described by the physiologists above mentioned, but so long as it can be demonstrated that the blood is in motion in the capillaries, it appears more philosophical to admit its influence in conveying the poison than to ascribe the transportation to another force. The following experiments will, I think, show that the power of imbibition is not so great as MM. Martin-Magron and Buisson contend.

Experiment. A large frog was selected, and a ligature was

placed around the large vessels of the lower part of the abdomen. The animal was then so arranged that both posterior extremities, as high as the middle of the legs, were kept immersed in a strong solution of the upas. At the end of an hour the chest was opened, and the heart was found to be actively pulsating. Six hours were suffered to elapse—the animal being retained in the same condition—and no symptoms of poisoning having been induced, it was released. The ligature was now removed from the vessels, and in the space of three minutes the heart had ceased to beat. Tetanus supervened a few minutes subsequently.

Experiment. The hind legs of a large frog were immersed in the same solution used in the foregoing experiment, and in a similar manner, except that no ligature was applied to the vessels, and that all the tissues but the vessels were entirely divided at about the middle of the thighs. The chest was then opened. The heart ceased to act in a little more than six minutes after the immersion, and after about eleven minutes had elapsed, the animal was in violent tetanic spasms.

As the objects of the present memoir relate solely to the action of the upas in my possession, it would be out of place to enter into any discussion of the investigations of MM. Martin-Magron and Buisson; but the two experiments above cited are at least indicative of the fact that the poison used exerted its influence solely through the circulation, and the other facts stated are, I think, strongly suggestive of errors into which these observers have fallen. At some future time I purpose considering their researches more at length. I would only say further, therefore, that the time the frogs used by these experimenters survived extirpation or ligature of the heart is altogether unprecedented, no observer, to my knowledge, ever having witnessed such lengthened vitality as that asserted by MM. Martin-Magron and Buisson to have attended their experiments under the above-named circumstances.

In its effects upon the nervous system, the poison under consideration is peculiar. Owing to the rapidity with which tetanus supervenes, it is impossible to determine when the voluntary movements entirely cease, even in frogs and other cold-blooded animals. In mammals and birds, these actions are of course very soon lost. In regard to the reflex actions, it is hardly necessary to state that they are greatly intensified. They also are manifested for a much longer period than in animals poisoned with corroval or vao, or in which the circulation has been arrested by ligation or excision of the heart. The following experiment, which is only one of many which were performed with reference to this point, is adduced:—

Experiment. A large frog was inoculated with the solution of the poison under the skin of the back at 11 A.M. At 11·6 the heart stopped. The animal was capable of voluntary actions till 11·13, when tetanus of a very violent character occurred. This condition was present in all its primary intensity till 12·20, when it began to exhibit a less violent character. At 2·30 general spasms were induced by the galvanic irritation of a posterior extremity, and even at 4 o'clock, under similar excitation, there were slight reflex actions caused in the muscles of the anterior extremities.

It is extremely probable that, like corroval in its relations to strychnia, the two poisonous principles of the upas are, to a certain extent, antagonistic, and I regret again that I had not sufficient of the heart-paralyzing agent to admit of my establishing this point as a certainty.

In its effects upon nervous and muscular irritability, the poison under consideration is more closely allied to strychnia than to corroval or antiar, *i.e.* the action of the strychnia is predominant over that of the other principle, and consequently the nerves and muscles retain their excitability for a longer period than when either of the two above-named substances is introduced into the circulation. Without giving the details of the experiments, I

would state, as the results of my investigations, that in frogs the nerves retain their irritability for about five hours, and the muscles for about an hour longer.

When taken into the stomach, the two principal actions of the poison are reversed in the order of occurrence. Tetanus first occurs, and it is not for some time afterward that the heart stops beating.

Experiment. Ten drops of the solution of the poison were introduced through a tube into the stomach of a large frog at 10·20. Tetanic spasms commenced at 10·32, and at 10 40 were at their height. The chest was opened, and the heart was found to be actively pulsating. It continued to beat till 10·58, when it stopped.

Experiment. Twenty-five drops of the solution were injected through a tube into the stomach of a small dog. At 12·5 the chest was opened and artificial respiration instituted. Tetanus supervened at 12·13. The heart continued acting till 12·28, when it stopped.

I found, by subsequent investigation, that it was possible to entirely prevent the paralysis of the heart by washing out the stomach a few minutes after the introduction of the poison. This is shown by the following experiment:—

Experiment. Ten drops of the solution of the poison were placed in the stomach of a frog at 2·15. At 2·20, before tetanic spasms had become developed, the stomach of the animal was inverted, and thoroughly washed with tepid water. It was then returned to its normal position. During the operation, tetanus supervened. The chest of the animal was opened, and the heart was found pulsating actively. It continued beating for several hours, during the whole of which time the convulsions were excited on the least irritation.

Introduced into the rectum, the effects ensue in the same sequence as when the poison is placed in the stomach, but with

somewhat greater rapidity. It may, therefore, be concluded that the mucous membrane of the alimentary canal is a better endosmometer for the solution of strychnia than for that of the heart-paralyzing agent.

Placed upon the skin of frogs, the poison produces similar effects to those which follow its insertion under the skin, and with almost as much rapidity. It is, perhaps, hardly necessary to cite any of the numerous experiments which were performed with reference to this point.

It was intended to have made these investigations much more extensive, but the limited quantity of the poison at my disposal prevented me doing as complete justice to the subject as I desired. From the researches, so far as they extend, I think it may be fairly concluded that the poisonous substance to which they relate is altogether different from any one species of poison heretofore described, and that while in many respects it is similar in physiological effects to both the upas antiar and the upas tieute in their joint actions, there is much reason for hesitating to regard it as a compound of these substances.

FURTHER EXPERIMENTS

RELATING TO THE

DIURETIC ACTION OF COLCHICUM.

IN the Proceedings of the Academy of Natural Sciences of Philadelphia for November, 1858, I gave the results of a series of investigations relative to the diuretic properties of digitalis, juniper, squill, and colchicum, by which it was shown that the latter alone possesses the power of increasing the amount of organic matter eliminated by the kidneys. From this circumstance, the argument was adduced that this substance, of all those experimented with, was the only one that could be regarded as a true depurator of the blood.

The results obtained by earlier investigators cannot be regarded as satisfactory, owing to the faulty manner in which their analyses were made. The urine was concentrated by heat, and thus a large quantity of its organic matter underwent decomposition.

Since the publication of my experiments, Dr. Garrod, of London, has studied the physiological action of colchicum; but, led away by his theory of the nature of gout, he limited his researches mainly to the determination of its influence over the excretion of uric acid, which, as is well known, forms but a small proportion of the total amount of organic matter excreted by the kidneys. As the result of his investigations, he announced that colchicum does not increase the quantity of uric acid contained in the urine, and that it is not by any action on the kidneys that the remedy in

question exerts its curative influence in gout. His result, as relates to the uric acid, does not, so far as I know, conflict with mine, as I did not separately determine the quantity of this substance present; but his conclusion, that colchicum is not a diuretic in the true sense of the term, is certainly not borne out by his own experiments, and is directly at variance with those which I performed.

It was, therefore, obviously necessary that additional investigations should be instituted, and I accordingly undertook the task of furnishing further contributions to the subject. Before proceeding to detail these, I desire to call attention to the valuable memoir of Professor Austin Flint, in the *American Medical Monthly* for November, 1860, entitled *Clinical Researches on the Action of Diuretic Remedies*. In this essay, in addition to much other valuable matter, the conclusion at which I had arrived relative to the action of colchicum is confirmed; Professor Flint finding it to produce a marked increase in the amount of solid matter eliminated by the kidneys, without, however, increasing the quantity of water of the urine.

The investigations to which the present paper relates consisted of experiments upon adult males, in a good condition of health. In all cases, the officinal tincture of the seeds of the *colchicum autumnale* was given.

The determinations made were the following: 1st, the quantity of urine; 2d, its specific gravity; 3d, the total amount of solid matter; 4th, the quantity of inorganic matter; 5th, the quantity of organic matter; 6th, the amount of uric acid.

The quantity of urine was determined in cubic centimetres.

The specific gravity was ascertained by means of the specific gravity bottle and a delicate balance.

The total amount of solid matter is given in grammes, and was determined in the following manner: Ten cubic centimetres of the urine were evaporated to as complete dryness as possible in

vacuo over sulphuric acid, and the residue accurately weighed. By simple proportion, the amount of solids in the whole quantity of urine was easily ascertained.

Although it is impossible to get rid of all the water by this process, the quantity remaining is extremely small, and the results obtained are far more accurate than those received by evaporating to dryness in the water-bath, as generally practiced. No matter how carefully this latter process is conducted, the loss of urea by decomposition is always an important item, and involves far more serious errors than the imperfect desiccation by the former process.

For the determination of the amount of organic and inorganic matter separately, the solid residue obtained as above was mixed with ten or fifteen drops of moderately strong nitric acid, and gently heated till the mass was well dried. The heat was then gradually raised till all the carbon was consumed, and the mass, in consequence, became white. It was then cooled *in vacuo* over sulphuric acid, and weighed. The inorganic matter was thus determined, and the loss showed the proportion of organic substance.

The quantity of uric acid was determined by adding chlorhydric acid to a known volume of urine.

The first experiments were instituted upon myself. In three days immediately preceding their commencement, the average quantity of urine for each day was 1425 cubic centimetres, of specific gravity 1021.73. The average amount of solid matter was 64.28 grammes; of which 30.18 were inorganic, and 34.10 organic substance. The average amount of uric acid excreted for each period of twenty-four hours was 0.77 gramme.

During the experiments with the colchicum my manner of living was not materially altered from that of the three days above referred to; *i.e.* I ate the same food and took the same amount of exercise, and endeavored to make all the collateral circum-

stances the same, so as to ascertain as nearly as possible the exact effect produced by the colchicum.

First Day.—On this day I took one fluid drachm of the tincture three times: at 8 A.M., 2 P.M., and 10 P.M. The total quantity of urine excreted was 1685 cubic centimetres, of which the specific gravity was 1021.50. The total amount of solids was 70.15 grammes, of which 30.90 were represented by inorganic, and 39.25 by organic matter. The quantity of uric acid was 0.81 gramme.

Second Day.—One and a half fluid drachms of the tincture were taken, as on the previous day. Quantity of urine, 1720 cubic centimetres; specific gravity, 1020.87; total solids, 75.29 grammes; inorganic solids, 32.44 grammes; organic solids, 42.85 grammes; uric acid, 0.69 gramme.

Third Day.—Same quantity of colchicum taken as on previous day. Quantity of urine, 1784 cubic centimetres; specific gravity, 1022.57; total solids, 80.13 grammes; inorganic solids, 35.11 grammes; organic solids, 45.03 grammes; uric acid, 0.82 gramme.

Fourth Day.—On this day the quantity of colchicum was reduced to half a fluid drachm, taken as before. Quantity of urine, 1540 cubic centimetres; specific gravity, 1023.17; total solids, 69.23 grammes; inorganic solids, 31.09; organic solids, 38.14 grammes; uric acid, 0.78 gramme.

Fifth Day.—On this day the quantity of colchicum was increased to one and a half fluid drachms of the tincture before mentioned. Quantity of urine, 1698 cubic centimetres; specific gravity, 1023.68; total solids, 76.14 grammes; inorganic solids, 33.26 grammes; organic solids, 42.88 grammes; uric acid, 0.76 gramme. On this day there was some derangement of the general health, manifested by increased heat of skin, fever, and severe abdominal pains. There was also a little diarrhoea. The experiments were therefore discontinued.

From an examination of the results obtained by the foregoing

investigations, the effect of the colchicum upon the urinary excretion cannot fail to be perceived. The conclusions which I think may be formed are: 1st. That the colchicum increases the quantity of urine. 2d. That it increases the total amount of solid matter eliminated. 3d. That this increase is mainly due to an augmentation of the organic matter. 4th. That the amount of uric acid does not appear to be affected.

These conclusions are rendered much more probable from the fact that on the fourth day, when the quantity of the tincture of colchicum taken was reduced one-third, the effect upon the urine was less decidedly marked; and that when, on the fifth day, it was again augmented to a drachm and a half, the urinary excretion was materially increased in quantity, and the solids, the organic especially, remarkably raised in amount. The relation of cause and effect would therefore appear to exist; and accordingly it would be contrary to the principles of sound reasoning to assert that the change in the composition of the urine was accidental. It is doubtless true that the urine changes greatly from day to day, and even from hour to hour; but this fact is due to the other fact, that we are constantly varying our food, exercise, etc. When, however, as in the investigations cited in this paper, these circumstances are fixed, and only one difference exists between the ordinary mode of living and that practiced during the continuance of the experiments, we are fairly justified in attributing any change in the urine or in any other excretion to the influence produced by that difference.

In the next series of experiments the effect is just as directly shown, though, for reasons beyond my control, they were not continued as long as was desirable.

The subject of these experiments was a young man twenty-three years of age, and weighing about 140 pounds. Before taking the colchicum, I examined his urine while he was taking a fixed quantity of food and exercise, he being at the time an

attendant in the hospital under my charge. As the results of these examinations for three consecutive days, I obtained the following as the averages for each day: Quantity of urine, 989 cubic centimetres; specific gravity, 1020·14; total solids, 51·20 grammes; inorganic solids, 22·45; organic solids, 28·75; uric acid, 0·47 gramme.

First Day.—On this day one drachm of the tincture of colchicum was taken three times. The effect upon the urine was as follows: Quantity, 1021 cubic centimetres; specific gravity, 1024·18; total solids, 63·25 grammes; inorganic solids, 23·57 grammes; organic solids, 40·68 grammes; uric acid, 0·59 gramme.

Second Day.—One and a half drachms of the tincture were taken to-day three times, as previously. Quantity of urine, 875 cubic centimetres; specific gravity, 1026·11; total solids, 60·25 grammes; inorganic solids, 20·38 grammes; organic solids, 39·87 grammes; uric acid, 0·51 gramme.

On this day diarrhœa was produced. This was of quite a severe character, and, in consequence, the colchicum was not further continued.

The remarkable effect of the colchicum in increasing the amount of organic matter excreted is, however, very decidedly shown. This increase is so great as to render the probability of its being accidental extremely small, and we cannot do otherwise than regard it as being directly due to the influence of the colchicum.

The details of the third case in which the colchicum was given have been unfortunately mislaid. I am, however, enabled to state with certainty, that the same well-marked effect over the amount of organic matter excreted by the kidneys was exerted as in the cases the particulars of which have been given in full. The experiments were continued for six days, with variable quantities of the tincture.

What are we to infer from these investigations? It appears

to me that the conclusion must be admitted that colchicum is a true depurator of the blood; and hence we have an explanation of its good effects in those blood diseases, gout and rheumatism.

It is seen that no constant effect was produced upon the quantity of uric acid eliminated; and hence these experiments do not conflict with those of Dr. Garrod. We are not, however, bound to admit that the presence of uric acid in the blood in increased amount during a paroxysm of gout or rheumatism, is the cause of that paroxysm; and consequently, because colchicum does not increase the quantity of this substance found in the urine, we are not to suppose that the remedy in question does not exert its influence through the kidneys.

URÆMIC INTOXICATION.

WHEN we consider how important a part the kidneys fulfil in depurating the blood, we can readily believe that any serious interruption to the due performance of their function must be attended by great disturbance in the healthy action of the other organs of the economy. We find that such is actually the case. Physiological experiments, together with many well-established cases of disease, have taught us that suppression of the urinary excretion is one of the most dangerous events that can happen in the whole range of pathological occurrences.

In the present memoir, I propose to consider the subject of uræmia, or that condition of system due to the accumulation in the blood of matters which in health are removed by the kidneys, basing what I have to say mainly upon my own investigations.

When the renal arteries of an animal—as, for instance, a dog—are ligated, or the kidneys removed, death ensues in from two to four days generally, though occasionally life is retained for a longer period. In one of my own experiments, the animal, a small dog, lived for twelve days; and Marchand* mentions a case in which a sheep lived for nearly a fortnight after removal of the organs in question.

At first, the animal upon which this operation has been performed does not appear to be seriously inconvenienced thereby. It eats, sleeps, and follows its other instincts with but little irregularity. After a variable period, noticeable symptoms begin to

* De l'existence de l'urée dans les parties de l'organisme animal autres que l'urine. *L'Experience*, 1839, tome ii. p. 43.

manifest themselves. These are loss of appetite, nausea, vomiting, and indisposition to exertion of any kind. Occasionally there is purging. Finally, there is either coma or convulsions, or both, and the animal dies in a state of stupor, or in epileptiform convulsions. If, previous to the death of the animal, the blood be examined, it is found loaded with urea, and this substance can generally be detected in the matters vomited and discharged *per anum*. *Post-mortem* examination reveals the presence of urea in the contents of the stomach, in the blood, the lungs, liver, and other parts of the body.

In Bright's disease, as it affects the human subject, we find that, owing to structural changes in the kidneys, the urine is imperfectly eliminated. An element—albumen—is separated from the blood, which does not normally exist in the urine. The excretion, upon analysis, is found to be deficient in urea, and may even, as I have myself found, be almost entirely free from it. Coma and convulsions at length appear, and death soon follows. If, previously to the above, the blood be analyzed, urea is discovered in large quantity, and a *post-mortem* examination reveals the presence of this substance in nearly every portion of the system. Such is the natural termination of Bright's disease. Sometimes, however, the retained elements of the urine, by their action on the brain and nervous system, produce inflammations of important structures, and death ensues before the stage of uræmic poisoning is reached.

In puerperal eclampsia, in the latter stages of scarlet fever, in yellow fever, and in cholera, symptoms and appearances similar to those above mentioned are frequently present, and probably depend upon a like immediate cause.

To these symptoms, taken collectively, the terms uræmia, uræmic intoxication, and others of like import have been applied.

Various theories have been propounded relative to the im-

mediate cause of uræmia. Thus, Osborne* considered it due to arachnitis; Prevost and Dumas† to effusion into the ventricles of the brain; Rees‡ thinks it may be caused by a watery state of the blood; and Bence Jones§ supposes it to be induced by an accumulation of oxalic acid in this fluid. There is no evidence to support any of these hypotheses; in fact, each has been positively disproved.

The view most generally held, has been that which ascribes uræmia to the direct action of the urea retained in the blood. Later investigations have called the correctness of this hypothesis in question, and much cogent evidence has been adduced against it. Like most other physiological questions, the present is not to be solved but by the patient and thorough research of numerous investigators. I can only hope that the observations and experiments which follow may prove to be contributions in the right direction.

The fact that urea is formed in the blood may be regarded as sufficiently determined. It is not present in the muscles, for analysis fails to detect it; but other substances, the immediate products of their destructive metamorphosis, and which admit of still further degradation, are found; and the experimental evidence, which establishes the fact that increased muscular exertion leads to increased elimination of urea, indicates these organs as one, at least, of its sources of origin. In addition, we have the beautiful researches of Bechamp,|| which are conclusive as to its production from proteinaceous substances.

* On the Nature and Treatment of Dropsical Diseases. London, 1837, p. 36.

† Annales de Chimie et de Physique, tome xxiii. p. 90 et seq.

‡ On the Nature and Treatment of Diseases of the Kidneys, etc. London, 1850, p. 67.

§ Lectures on Animal Chemistry. Medical Times, January 3, 1852.

|| Annales de Chim. et de Phys. November, 1856. Since the above was written, doubt has been cast upon the correctness of Bechamp's results and deductions; admitting, however, their erroneous character, there is still ample proof of the origin of urea.

Prevost and Dumas,* Marchand,† and numerous other observers have shown that, after extirpation of the kidneys, urea accumulates in the blood, and consequently these organs cannot be regarded as forming this substance. They, in fact, only separate it, as they do the other constituents of the urine, from the blood brought to them by the renal arteries. As the healthy kidneys are constantly in action, urea never normally exists in the blood in any very considerable amount. It is only when, through disease or other cause, the kidneys are prevented performing their function of elimination, or when large quantities are submitted to examination, that urea is to be detected in the blood in any but very small proportion.

The immediate cause of the production of the group of symptoms known as uræmia is at present, as has been already stated, a point upon which there exists some diversity of opinion, though numerous researches have been made with the view of elucidating the subject. Urea has been injected into the blood of animals, and as death did not often follow, this substance has been regarded by some as non-poisonous. Even urine, filtered so as to free it from mucus and epithelium, has, under like circumstances, proved harmless; but when injected unfiltered, death invariably ensued. The inference, therefore, from these last cited experiments is, that the urine, if not eliminated, is not, as such, capable of causing death, for the mucus and epithelium are not separated from the blood by the kidneys, and consequently are not, properly speaking, constituents of the urine. As, however, the injection of unfiltered urine has always resulted in death, the further deductions must be drawn that epithelium, or mucus, or both, are of themselves poisonous, or that one or both are capable of so acting upon the retained elements of the urine as to cause the formation

* *Annales de Chim. et de Phys.*, 1823, tome xxiii. p. 90.

† *L'Experience*, 1839, tome ii. p. 43.

of some substance possessed of toxical properties. These conclusions are, however, of course only legitimate, provided that the experiments referred to have been conducted with the care and accuracy so absolutely essential in all physiological investigations. It will be seen hereafter that it is more than probable the experiments cited were not altogether free from error.

In a philosophical treatise on the subject of Bright's disease, Frerichs* advances the opinion that uræmia is not due directly to the presence of urea in the blood, but to the conversion of this substance into carbonate of ammonia, through the agency of a ferment supposed to be present in the circulating fluid. This view has been accepted by Braun,† but has been controverted by Schottin,‡ Zimmerman,§ Gallois,|| myself,¶ Bernard,** and others.

The arguments relied upon by Frerichs to support his theory are based mainly upon experiments on the lower animals—dogs—but partly upon observation of cases of Bright's disease which came under his notice. As this hypothesis, from the source whence it comes, from its apparent simplicity, and from certain facts which seem to give it support, has attracted to a considerable extent the attention of pathologists, I deem it important,

* Die Brightsche Nierenkrankheit und deren Behandlung. Braunschweig, 1851, p. 111.

† The Uræmic Convulsions of Pregnancy, Parturition, and Childbed. Edinburgh edition, 1857. Translated by Dr. J. Mathew Duncan, p. 16. I regret that I have not the original work (Lehrbuch der Geburtshülfe, u. s. w. Wien, 1857) to refer to. Dr. Duncan's translation, however, appears to be very correctly rendered.

‡ Vierordt's Archiv, 1853, Heft i. p. 170.

§ British and Foreign Medico-Chirurgical Review. Am. ed., January, 1853, p. 223. From Deutsche Klinik, No. 37.

|| Comptes Rendus, No. 14, Avril, 1857.

¶ On the Injection of Urea and other substances into the Blood. North American Medico-Chirurgical Review, April, 1858.

** Leçons sur les Propriétés Physiologiques et les Altérations Pathologiques des Liquides de l'Organisme, tome ii. Paris, 1859, p. 36.

before proceeding further, to enter somewhat at length into its consideration.

The fact that urea may be injected into the blood without uræmia following, and that even filtered urine may be thus introduced with impunity, are circumstances considered by Frerichs as incompatible with the hypothesis which ascribes this condition to the retention of the urea *per se*. That in animals, the kidneys of which have been removed, there was vomiting and purging of ammoniacal matters; that ammonia was exhaled from the lungs, and that after death, as well in them as in persons dying of Bright's disease, who during life had manifested symptoms of uræmia, ammonia was discovered in the blood and in the contents of the stomach and intestines; that urea has been frequently found in the blood of persons suffering from Bright's disease, in whom no uræmia was present, and *vice versa*,—constitute, in his opinion, a mass of evidence strongly in favor of the theory he has advanced. Add to all this the results of experiments performed by him with direct reference to the point in question, and we have the main points before us upon which he has constructed the ingenious and beautiful hypothesis, that uræmic intoxication is directly due to the presence of carbonate of ammonia in the blood, which substance has been formed from the retained urea through the action of a ferment. Of the nature of this ferment he does not attempt to furnish an explanation.

Two series of experiments were performed by Frerichs. In the first, a solution containing from two to three grammes of urea (thirty-one to forty-six grains) was injected into the veins of dogs, the kidneys of which had been previously removed. The animals remained for some hours to all appearance unaffected; a circumstance which Frerichs regards as indicating that the urea, as such, exerted no detrimental influence upon the nervous system. After a longer or shorter period, (from one and a quarter to eight hours,) the animals became restless, and vomited acid chyme, or a

mucous matter of a yellow color, according as the stomach was full or empty at the commencement of the experiments. Under the latter condition, the vomited matter was of decided alkaline reaction. Convulsions occurred, and, at the same time, ammonia was expelled with the expired air. Finally, the animals fell into a state of coma, the respiration became stertorous, and death soon followed. Occasionally the convulsions were absent, coma being the first symptom of cerebral disturbance. After death, which generally occurred in from two and a half to ten hours after the injection of the urine, ammonia was always found in the blood. The contents of the stomach, in most instances, gave off a strong ammoniacal odor, and contained carbonate of ammonia in large quantity. In one case they were feebly acid, and even then ammonia was present. This substance was also found in the bile and other secretions.

In the second series of experiments, a solution of carbonate of ammonia was injected into the circulation, the kidneys of the animals remaining intact. Immediately afterward convulsions ensued, which, in some cases, were very violent, but were soon succeeded by a comatose condition. The respiration was laborious, and the expired air was loaded with ammonia. There was also vomiting of biliary matters. The stupor lasted for several hours; so long as it was present, ammonia continued to be exhaled from the lungs. Gradually it ceased to be expired, and the animals slowly recovered their senses. If, during the coma, an additional amount of carbonate of ammonia was injected, convulsions again occurred, the vomiting was renewed, and the urine and feces were involuntarily evacuated. In from five to six hours, the ammonia again disappeared from the blood, and the animals regained their ordinary liveliness.*

There are several objections to be urged against these experi-

* *Op. cit.*, p. 111 et seq.

ments of Frerichs, and the inferences drawn from them by him and those who coincide with him in his uræmic theory. In order to present these more connectedly and with greater clearness, I quote Frerichs's own details of the first experiment of each series, which may be taken as the type of the others of its class. The first series consisted of six experiments:—

“No. 1. Both kidneys were extirpated from a young full-grown dog, at 3 o'clock P.M., by opening the abdominal cavity. On the following morning the animal appeared to be perfectly well; it ate, and wagged its tail when spoken to. The posterior extremities, however, appeared to be paralyzed. At 3 P.M. a solution of two grammes of urea was injected into the left jugular vein. The animal remained in the same state as before, its condition not being altered in the least. At 4 P.M. it became restless, seemed to be choking, and vomited several times. The matter thus ejected consisted of a slimy yellow fluid, with a strong alkaline reaction. Soon afterward convulsions supervened, the animal rolled from one side to the other. Opisthotonos ensued in the posterior, alternating with violent contractions of the other muscles of the body. From time to time the animal was quiet, after which the convulsions returned with increased violence. In the mean while the vomiting continued, and a glass rod, moistened with chlorhydric acid, and held to the nose, caused the formation of thick white fumes, showing the presence of ammonia in the expired air. By degrees the convulsions abated in violence, and at length entirely ceased. The animal now lay in a state of sopor, the respiration being quick and difficult. Finally, the respiratory motions became weaker, and at 5½ P.M. death ensued.

“The cavities of the body were immediately opened, and the blood contained in the heart and large vessels collected. It was of a dark-violet color. The color did not become markedly clear by heating, but by the following morning it had assumed a bright-scarlet hue. After four minutes the fibrin was strongly coag-

ulated. The blood corpuscles were not changed from the normal form. Ammonia in considerable quantity was contained in the blood—a glass rod previously moistened with chlorhydric acid giving rise to the white fumes indicative of its presence.

“A part of the defibrinated blood was mixed with water, and distilled in the water-bath. A fluid with an alkaline reaction came over, which, being neutralized with chlorhydric acid and evaporated, deposited crystals of chloride of ammonium. To another part of the blood caustic potash was added, and an ammoniacal odor was given off.

“The stomach was strongly contracted, and contained still a few corroded pieces of bone, and a small quantity of a yellow, tenacious, ropy fluid. The stomachal mucous membrane was of a livid-red color, partly through vascular injection and partly through imbibition. The fluid contained in the viscus exhaled a sharp odor of ammonia, reacted strongly alkaline, and formed thick fumes with chlorhydric acid. In an alcoholic extract of the same, no traces of unconverted urea were discovered. In the bile also urea was sought for, but only compounds of ammonia were detected. The substance of the brain and the membranes covering it contained the normal quantity of blood, and the fluid in the ventricles was not increased in amount. The lungs were healthy, except that posteriorly there was some congestion. The mucous membrane of the trachea and bronchia was slightly reddened. The liver and spleen were to all appearance healthy. In the abdominal cavity a small quantity of bloody fluid was contained. No evidences of intense peritonitis were visible.”*

The other experiments of this series do not differ in any material respect from the one quoted, except that in the third no ammonia was detected in the expired air. The details of the fifth and sixth are not given.

* *Op. cit.*, p. 278 et seq.

Now in these experiments there is not the least evidence that carbonate of ammonia was the cause of death, or even that this substance was present in the blood in any abnormal amount.

In the first place, it is asserted that ammonia was present in the pulmonary exhalation. This statement is doubtless correct, but the inference which Frerichs draws from it is, I think, unwarranted. Ammonia can generally be detected in the products of respiration in healthy dogs, into the veins of which no urea has been introduced, and in which the kidneys are in healthy functional activity, by employing the test made use of by Frerichs. It is, however, occasionally absent, and in several cases which will hereafter be more specifically referred to, in which urea had been introduced directly into the blood, ammonia was not to be found in the pulmonary exhalation, though recourse was had not only to Frerichs's process, but to others of far greater delicacy.

In the second place, the means employed by Frerichs to establish the existence of ammonia in the blood were faulty in the extreme, and such as will always effect this object if urea be present, even though ammonia, in the first instance, be altogether absent. The defibrinated blood was distilled in a water-bath, (at what temperature we are not informed,) and an ammoniacal fluid collected. Now no matter how carefully this operation was conducted, if any urea was present, a portion of it would have undergone decomposition, and ammonia would have appeared in the distillate.

Thus, I took about thirty cubic centimetres of freshly-drawn dog's blood, defibrinated it by shaking it in a bottle with small strips of lead, and then added to it five grammes of urea. It was then placed in a small retort, and carefully distilled in the water-bath at a temperature of 85° Cent. (185° F.) till a sufficient quantity had passed over. A few drops of the distillate were then placed on a strip of glass, and held for a few moments over a vessel containing chlorhydric acid. Upon evaporation, and

subsequent microscopical examination, crystals of chloride of ammonium were found in large quantity. A similar strip of glass was then exposed to the vapor of chlorhydric acid, and held for a short time to the beak of the retort, while the distillation was progressing, in such a manner that the vapor was received upon it. Thick white fumes of chloride of ammonium were produced, and crystals of the same substance were formed upon the glass.

In order further to establish the presence of ammonia, Frerichs added caustic potash to another portion of the blood. This proceeding was equally objectionable as the other, for this substance decomposes urea into carbonate of ammonia, and of course therefore it was not surprising that an ammoniacal odor should have been evolved.

Now I have no intention of denying that ammonia existed in the blood of the dogs submitted by Frerichs to experiment. On the contrary, I believe it to be generally present in the blood of most animals. The fact that Frerichs detected it by holding over the blood a glass rod moistened with chlorhydric acid, is perhaps sufficient to establish the point. But that this circumstance is at all confirmatory of his theory is far from being the case. Richardson* has shown, by numerous experiments, that ammonia is a constant constituent of the blood of dogs and many other animals, and by repeated observations I have satisfied myself of the correctness of this conclusion. I have frequently failed when using Frerichs's test with the glass rod moistened with chlorhydric acid, which, besides its want of extreme delicacy, is liable, from several causes, to yield erroneous results. These, however, with care may generally be avoided. I have, therefore, preferred either Reuling's† process with logwood, or Richardson's, which consists

* The Cause of the Coagulation of the Blood. Astley Cooper Prize Essay for 1856. London, 1858.

† Archiv des Vereins für gemeinschaftliche Arbeiten, Zweiter B., 1856, S. 120.

in moistening a slip of glass with chlorhydric acid, and exposing it to the vapor arising from the blood, when, if ammonia be present, minute crystals of chloride of ammonium will be formed, and may be readily perceived under the microscope, with an object-glass of moderate power. This process has already been referred to as the means employed during the present researches in examining for ammonia.

I am aware that Davy* has not been able to detect ammonia in the blood of the common fowl. Not having access at present to the original paper, I know not what process he employed. With Richardson's method, I have never failed to find it in the blood of this animal in the course of fourteen experiments with reference to this point.

It will be seen, therefore, that ammonia is not an abnormal constituent of the blood, as Frerichs evidently supposes. There is no proof either that any of the retained urea was converted while in the system into carbonate of ammonia.

The fact that ammonia was found in the contents of the stomach, which consisted of fragments of undigested bone and of mucus, should not have the least weight in the matter, as it is well known that this latter substance causes the decomposition of urea, and the consequent formation of ammonia. No urea was detected in the alcoholic extract of these contents, and it is therefore probable that it was, as Frerichs supposes, entirely decomposed. There is no evidence, however, to lead us to infer that this change was effected in the blood, but, on the contrary, much to warrant us in believing that it took place in the stomach, through the action of the mucus present in this viscus.

In support of this view, I adduce the following experiments:—

Experiment. To a full-grown dog, fasting, two grammes of

* North American Medico-Chirurgical Review, vol. iv. No. 1, 1860, p. 149. (From Dublin Quarterly Journal of Med. Science, November, 1859, p. 425.)

urea were administered dissolved in water. Fifteen minutes afterward the animal was killed by injecting a solution of woorara under the skin. The stomach was opened, and found to contain nothing but a quantity of thick, tenacious mucus, which exhaled a strong ammoniacal odor. On bringing a glass rod moistened with chlorhydric acid near it, the dense white fumes of chloride of ammonium were formed, and crystals of this substance appeared on a slip of glass used in the manner before specified.

Experiment. To another dog, somewhat smaller than the first, five grammes of urea were given in the same manner as before, and at the end of ten minutes the animal was killed by dividing the medulla oblongata. The stomach was immediately opened. It contained a few fragments of bone, some pieces of undigested meat, and a quantity of thick mucus. The mass was of feeble alkaline reaction, and evolved a barely perceptible ammoniacal odor. The presence of ammonia was further established, as in the first instance.

The contents were then examined for urea by the process hereafter detailed, and this substance was shown to be present in considerable amount. Owing to an accident, it was not weighed.

If, however, the animal has eaten largely a short time previous to the injection of the urea, the change into carbonate of ammonia does not occur, and if the animal be killed soon after the administration of the urea, this substance is found intact in the stomach. If, however, sufficient time has elapsed, it is absorbed into the circulation and excreted by the kidneys.

The following experiments are adduced, as tending to establish these propositions:—

Experiment. A full-grown dog was fed largely on animal food, and thirty minutes afterward two grammes of urea administered to it. Fifteen minutes after taking the urea it was killed by section of the medulla oblongata. The contents of the stomach were of acid reaction. On testing for ammonia by Richardson's

method, a negative result was obtained. Neither were fumes of chloride of ammonium formed by the proximity of chlorhydric acid.

Experiment. A full-grown dog was confined and fed during three days on raw beef, two and a half pounds being given to him in the twenty-four hours. A uniform quantity of water was allowed. The urine of each period of twenty-four hours was collected, and tested for urea by Liebig's process with the nitrate of mercury. On the fourth day the animal was fed as before, but with each meal two grammes of urea were administered. Six grammes were administered in all. The immediate effect was to increase to a considerable extent the amount of urine eliminated, which contained an augmented quantity of urea. The following table exhibits the results:—

	1st day.	2d day.	3d day.	4th day.
Quantity of urine..	815 c. cm.	795 c. cm.	891 c. cm.	1073 c. cm.
Urea.....	15.25 gram.	14.75 gram.	15.10 gram.	20.22 gram.

Gallois,* from experiments on rabbits, arrived at a similar conclusion, and has also shown that urea acts as a violent poison on these animals when injected into the stomach in sufficiently large amount. A train of symptoms was induced similar to those of uræmia, of which the animals died. During the progress of these symptoms, there was no ammonia in the breath.

I cannot therefore perceive, from a consideration of Frerichs's experiments, and from those performed by myself as well as from the other evidence adduced, that there are any facts to warrant us in concluding that urea is transformed while in the blood into carbonate of ammonia.

As has been already stated, Frerichs performed another series of experiments, in which the carbonate of ammonia was directly introduced into the blood. In this series a filtered solution, con-

* Op. cit.

taining from one to two grammes of the carbonate, was employed. The first experiment, from which the others do not materially differ, is detailed by Frerichs as follows:—

“No. 1. Into the jugular vein of a strong, full-grown dog the solution was very slowly injected. The dog moaned and fell into deep stupor, broken occasionally by convulsions. The respiration was quickened, and the expired air was loaded with ammonia. The coma lasted for three hours, after which the animal regained its ordinary liveliness. During the coma, ineffectual efforts to vomit twice occurred.”

The experiments of this series amounted to six in number. None of the animals subjected to them died—a fact which, to say the least, is not one calculated to support Frerichs's hypothesis.

That carbonate of ammonia, when introduced directly into the circulation, produces considerable disturbance in the phenomena of life is doubtless correct. It is, however, excreted so rapidly by the lungs that the most enormous quantity may be injected without death ensuing. Thus Dr. Steiner,* late of the United States army, performed some years since a series of experiments, some of which show this very strikingly. In one instance, two ounces of strong aqua ammoniæ, diluted with an equal amount of water, were introduced into the circulation of a horse, and although the animal suffered severely for a few minutes, it soon rose from its feet, and trotted about as though nothing had happened.

I have myself† also experimented with reference to this point, and have injected as much as sixty grains of carbonate of ammonia into the jugular vein of a dog in normal condition. Convulsions ensued, and ammonia was exhaled from the lungs. The animal, however, recovered perfectly in a short time. Urea was

* Medical Examiner, vol. v. No. 11, N. S., 1849, p. 644.

† North American Medico-Chirurgical Review, vol. ii. p. 291.

also injected with a like ultimate result. The symptoms observed were, however, by no means identical in both cases.

In a second series of experiments performed, and detailed in the same memoir, the kidneys were removed, and in these animals death followed in a few hours after the injection of ammonia and other substances. From these experiments it is apparent that carbonate of ammonia possesses no pre-eminence as a toxical agent over substances not regarded as poisonous. The investigations, however, are not sufficiently extensive to warrant the formation of decided conclusions from them. It is nevertheless perceived that when urea was injected it was not decomposed into carbonate of ammonia either in unmutilated dogs or in those deprived of their kidneys.

In Bright's disease, there is a condition of system present very similar to that existing in animals the kidneys of which have been removed. In persons, therefore, suffering from this affection, carbonate of ammonia, if injected in large quantity into the blood, might cause death, or, even if retained in this fluid to any very great extent, the same result might follow. As, however, we have no proof that there is any accumulation of this substance in the blood during the progress of the disease in question, we cannot ascribe uræmic intoxication to its influence.

In the breath of persons laboring under Bright's disease, Frerichs constantly detected ammonia, and this circumstance is advanced as an additional argument in favor of his hypothesis. Allusion has already been made to the fact that ammonia can generally be found in the pulmonary exhalation of dogs. It is perhaps even a more constant constituent of the human breath, even in that of persons who, as far as can be perceived, are in perfect health. Richardson,* in many examinations, failed to find it only in one person. Schottin† detected it in the breath of

* *Op. cit.*

† Vierordt's Archiv. 1853, Heft i. s. 170.

persons suffering under other affections than Bright's disease, and in sixteen cases of uræmic poisoning found ammonia in the breath but once, and then, he thinks, it was probably derived from the mouth.

Mettenheimer* found white fumes produced by a rod moistened with chlorhydric acid, as readily with the breath of healthy persons as with that of subjects of uræmia; and, in a note to his memoir, Beneke states that he has arrived at similar results. Viale and Latini,† by numerous delicate experiments, have also shown that with each act of expiration ammonia is exhaled from the lungs of the healthy human subject.

From my own investigations, it has resulted that I have scarcely ever failed to find ammonia in my own breath, or in that of very many healthy persons whom I have examined.

I have thus considered, at some length, the arguments and experiments brought forward by Frerichs in support of his theory, and have, I think, sufficiently shown that it is not tenable. It is because, if generally adopted, it may lead to very grave errors in diagnosis and practice, that I have deemed it important to show how many facts tend to disprove the hypothesis in question.

Another view of the cause of uræmia, inferentially supported by Bernard,‡ requires some notice. According to this hypothesis, the condition in question is produced by decomposition of the tissue of the kidneys, and the retention in the blood of the elements arising from their putridity. The experiments of Müller and Peipers,§ and of Marchand,|| are adduced as tending to

* Archiv des Vereins für gemeinschaftliche Arbeiten, u. s. w. Band i. Heft iv. 1854, p. 605.

† American Journal of the Medical Sciences, April, 1855, p. 488. From L'Union Médicale, tome viii. No. 98, Août, 1854.

‡ Leçons sur les Propriétés Physiologiques et les Alterations Pathologiques des Liquides de l'Organisme. Paris, 1859, tome ii. p. 34 et seq.

§ Archiv für Physiologie, 1836.

|| Journal für practische Chemie, Band xi. s. 149.

establish the correctness of this theory. These observers induced mortification of the kidneys by ligating the renal nerves, and though it is asserted that death ensued from uræmia, it is by no means clear that this condition was not due to the cessation of the function of the kidneys rather than to the entrance into the blood of septic matters from the mortified organs. Moreover, when the kidneys of an animal are removed, there is certainly no retention in the blood of putrid matters arising from their decomposition, and yet death invariably follows. The entrance into the blood of substances in a state of putrefactive fermentation would more probably induce a pyæmic or typhoid condition of the system than one of uræmia. Finally, in Bright's disease, of which uræmia so frequently forms a prominent concomitant, pathology shows that the existing condition of the kidneys is not one at all analogous to putrefaction.

It is perhaps unnecessary to consider other objections which are applicable to this hypothesis.

The theory which much observation and numerous experiments have led me to think most probably correct, is that which ascribes uræmic intoxication to the direct action of the elements of the urine retained in the blood upon the brain and nervous system, in a manner which we do not at present understand. Of these elements, we have strong reasons for deeming urea the most poisonous.

It is true that urea has been directly introduced into the circulation of healthy animals without death ensuing. Thus Vauquelin and Segalas* injected a solution of this substance into the veins of dogs and cats, without the production of any remarkable effect other than an increase in the amount of urine excreted. They then injected urine, and death followed with symptoms of uræmia. Hence they drew the conclusion that it is the urine as a whole which, when retained in the blood, induces toxication.

* Journal de Physiologie de Magendie, tome ii. p. 254.

Frerichs* thinks that death in these cases arose from the urine being unfiltered; that is, from the mucus and epithelium derived from the urinary passages. He has repeatedly injected from twenty to forty grammes of filtered urine, sometimes even adding urea to it, into the veins of animals, without causing death. An increased quantity of urine was evacuated, but the normal condition of the organism was not otherwise disturbed. A warm saturated solution of urate of soda likewise produced no untoward result. The amount of urea excreted by the kidneys was, however, greatly increased.

Other observations have also been made relative to the point in question, and leading to the same general conclusions. It may therefore be regarded as a well-established fact that urea, in considerable amount, may be introduced into the blood of healthy animals, without death being necessarily produced.

It has been definitely shown that urea is a normal constituent of the blood. It has been found in the chyle, the lymph, the saliva, the bile, the aqueous and vitreous humors, the perspiration, the liquor amnii, the fluid of blisters, in dropsical effusions, in fecal evacuations, and even in the milk. It cannot, therefore, be regarded as poisonous, unless when, from defective excretion, it accumulates in the blood.

The amount of urea formed within the organism is, as has already been shown, subject to very great variation; but so long as the kidneys continue to perform the function of elimination in accordance with the requirements of the system, the normal balance between the urea and the blood is not disturbed. Thus it is that urea, and even urine, may be directly introduced into the circulation without inducing continued uræmia; for so soon as these substances reach the kidneys—as Vauquelin and Segalas, Frerichs, and many other investigators have shown—there is an

* *Op. cit.* p. 106.

increased elimination of urine, they are expelled from the body, and the coma, convulsions, and other accompaniments of toxication cease.

Oceasionally it happens that when the kidneys do not properly depurate the blood, other organs assume their office, and then uræmic intoxication does not occur.

Several cases are on record in which, from total suppression of the function of the kidneys continuing for a long time, this condition existed. One of the most remarkable of these is that reported to the French Academy of Sciences, several years since, by Monte-Santo,* of Padua, the accuracy of whose statements was confirmed by MM. Graefe and Frank from personal observation. In the case in question, there was complete constipation of the bowels and suppression of urine for fourteen years. There was always vomiting in from two to five hours after each meal, and about once a month a large quantity of fecal matter was discharged in the same manner. Although it is stated that there was no odor of urine in these egesta, it is more than probable that the stomach vicariously performed the function of the kidneys, and perhaps the skin also shared with it this office. Some years previously, a case had been reported to the Academy, in which there had been no discharge of feces or urine—by the ordinary channels, at least—for a period of seventy-two years.

Whatever doubt may be attached to such cases as the above, it is very certain that in several diseases it frequently happens that other organs than the kidneys eliminate some of the elements of the urine from the blood. This is especially the case in Bright's disease, in yellow fever, and in cholera. Immediately previous to the accession, and during the continuance of the stage of collapse, in this last-named disease, the cutaneous transpiration often contains urea, which is deposited by evaporation on the

* *Medico-Chirurgical Review*, July, 1833, (American edition,) p. 236.

skin. I have frequently had occasion to notice this circumstance, and in one case in particular, which fell under my charge, the skin of the face, chest, and arms presented the appearance of being dusted with a fine white powder from the large quantity of urea which covered it. The urine contained scarcely a trace of this substance; but it was found both in the fluid vomited and that discharged *per anum*. I do not cite this case as one at all singular, but merely for the bearing which it has upon the subject under consideration. In the numerous cases of cholera which have fallen under my observation, I have generally, whenever an examination was instituted, detected urea in the rice-water discharges from the stomach and bowels.

The experiments of Bernard and Barreswil,* which show that when the kidneys are removed from an animal, urea is excreted by the gastro-intestinal canal, may also be adduced. These observers extirpated the kidneys from dogs, and found that in those animals which survived but a short time no urea was to be detected in the blood, but that the matters ejected by vomiting and purging contained large quantities of ammonia, the product of the decomposition of the urea through the action of mucus and other gastro-intestinal secretions. If, however, death did not soon follow, the stomach and intestines lost their vicarious office, and then urea was found in the blood.

The fact that urea may occasionally exist in large quantity in the blood without giving rise to uræmic intoxication, is no proof that this substance is not generally poisonous. No one will deny the poisonous properties of arsenic. Dr. Taylor† gives the opinion, that a medical witness would be justified in stating it to be fatal in doses of two or three grains, yet subsequently refers

* Sur les voies d'élimination de l'urée après l'extirpation des reins. Archives Générales de Médecine, 1847, tome xiii. p. 449; also, Leçons sur les Liquides de l'Organisme, etc., tome ii. p. 36.

† On Poisons. Second American edition, 1859, p. 341.

to cases in which half an ounce, an ounce and a half, and even two ounces, had been taken without causing death. In the first of these instances, there was not even vomiting. So in relation to opium, as small a quantity as four grains produced death in a robust man; while, on the other hand, as much as five ounces of laudanum has been taken without even causing sleep. Similar instances might be brought forward in relation to almost every other poisonous substance.

It may perhaps be objected, that in such cases the poisons were not absorbed into the blood; but toxic agents have been introduced directly into the circulation, and like differences in the extent of their action have ensued. I might bring forward numerous examples in support of this assertion, but it will probably be sufficient to recall the fact of the total insusceptibility of some persons to the action of the vaccine virus.

In Bright's disease, the disorganization of the kidneys is generally of slow progress. They continue to perform their function, though imperfectly, and consequently the amount of urea contained in the blood is not, in the first stages, very excessive. Its accumulation is gradual, and there is therefore time for the system to become in a measure habituated to its presence in such an amount that, if suddenly introduced into the blood and not eliminated, uræmia would in all probability ensue. We find this ability of the system to adapt itself to gradual changes generally present in all animals, and with reference to the action of poisonous substances exceedingly well marked. Thus, by progressively increasing the doses, large quantities of arsenic, opium, strychnia, hydrocyanic acid, and other toxic substances may be taken without the production of the least poisonous effect.

When, however, in Bright's disease, the structure of the kidneys becomes so greatly disorganized as to unfit them entirely for depurating the blood, the elements of the urine continue to accumulate, and, if not otherwise excreted, almost invariably give rise to uræmia.

As to the assertion that uræmic intoxication may exist without the accumulation of urea in the blood, I have only to say that there is no evidence whatever to support such a conclusion.

The following investigations were undertaken with the hope of being able to contribute somewhat to a fuller and more exact understanding of the cause of uræmia. I have endeavored to avoid every source of fallacy, and though—knowing the difficulties which attend researches of this character—I can perhaps scarcely assume to have succeeded, I am, nevertheless, unaware of any circumstances which would invalidate the conclusions drawn.

To say that I entered upon the inquiry without certain preconceived opinions, would be far from correct. That such views as I had conceived have, however, blinded me to the truth, or warped my judgment of things as they actually were, I do not believe. Theories are true but for the time being, and physiological hypotheses are even more ephemeral than any others. We should therefore be prepared to yield our convictions without regret, when they do not accord with the results of experiments better devised and more accurate than our own, for only by so doing can we entitle ourselves to be considered useful laborers in the fields of science.

The chemical processes used in the several determinations were as follows:—

In examining the *blood* for urea, a weighed portion was mixed with its volume of strong alcohol, and evaporated over sulphuric acid or chloride of calcium, *in vacuo*, to dryness. The residue was pulverized, and extracted with cold alcohol. The alcoholic extract was filtered, and carefully evaporated to dryness at a low temperature in the water-bath, and the residue washed repeatedly with small portions of ether. The ether extract was filtered and evaporated to dryness. Nitric acid was then added to the residue, the whole thrown upon a filter of known weight, and subjected to

strong pressure. It was then dried at 100° C., and weighed. The difference between the weight of the whole and that of the filter gave the amount of nitrate of urea, and from this the quantity of urea was calculated.

Whenever the amount of urea was too small to determine quantitatively, the dried ether extract last obtained, as in the foregoing process, was placed upon a glass slide, and nitric acid added to it under the microscope. The production of rhombic and hexagonal tablets, the opposite acute angles of which measured 82° , was deemed sufficient evidence of the presence of the substance sought for.

The same methods were used to determine the existence of urea in the vomited and fecal matters, whenever they were examined for it.

For ascertaining the amount of urea in the urine, Liebig's volumetric process with the protonitrate of mercury was always employed.

In the determination of ammonia, Richardson's process, already detailed, or Reuling's, was made use of. Whenever negative results were obtained by the one, recourse was always had to the other.

In the first place, I was desirous of ascertaining more definitely than had hitherto been done, the action of urea when injected into the blood of sound and healthy animals.

Experiment. A large adult dog, weighing 65 pounds, was fed for three days on fresh meat. During this period, ammonia was constantly found in the breath.

On the fourth day the jugular vein of the left side was opened, and a sufficient quantity of blood abstracted. One hundred grammes of this contained 0.019 gramme of urea. Ammonia was present, as it was likewise in the expired air.

The urine passed on this day amounted to 1025 cubic centimetres, and contained 11.28 grammes of urea.

The food was the same as on the preceding days.

On the morning of the fifth day, at 9 A.M., 3 grammes of urea, dissolved in 30 cubic cen. of distilled water, were injected into the jugular vein. The animal, from the very first, appeared to suffer pain. It moaned; the breathing became labored; and it trembled violently, as if from fright or cold. At the end of about twenty minutes, the animal became more quiet, and even appeared to be somewhat stupefied. After nearly an hour had elapsed, convulsions ensued. These were confined almost entirely to the posterior extremities, though at times the other portions of the body were in spasms.

At 10 o'clock, while the convulsions were still present, I abstracted 100 grammes of blood. It contained 0.135 gramme of urea. Ammonia was also present, though in no larger amount than on the previous day. Examined microscopically, the red blood corpuscles were found to be of normal size, shape, and color. They appeared, however, to be diminished in quantity. The white corpuscles were very evidently increased in amount.

The animal continued to be convulsed till about 2 o'clock P.M., when coma ensued. This lasted $3\frac{1}{2}$ hours. The dog then awoke, and passed a large quantity of urine. It amounted to 280 cubic centimetres, and contained 2.15 grammes of urea.

Before, during, and after the convulsions, ammonia was exhaled with the breath.

Immediately on the dog awaking, I again abstracted 100 cubic centimetres of blood from the jugular vein. This contained 0.014 of urea.

The total amount of urine voided on this day was 1381 cubic centimetres, containing 14.63 grammes of urea.

The dog ate as much on this day as on any previous one. It recovered perfectly.

Experiment. For this experiment, a dog, weighing $38\frac{1}{2}$ pounds, was used. As in the preceding experiment, it was fed for three

days on fresh meat. During this period, at only one examination—at 10 o'clock A.M. on the second day—was ammonia detected in the expired air. On the fourth day, 100 grammes of blood were abstracted from the jugular vein, and found to contain 0·027 gramme of urea. Ammonia was also present, and likewise in the pulmonary exhalation.

The urine voided on this day amounted to 834 cubic centimetres, and contained 4·09 grammes of urea.

On the fifth day, at 10 o'clock A.M., 5 grammes of urea, dissolved in 30 cubic centimetres of distilled water, were injected into the jugular vein. No immediate effect was produced. After the lapse of forty-five minutes, there were slight spasms of the muscles of the eyelids; and fifty minutes after the injection, a severe general convulsion ensued. The vein was now reopened, and 100 grammes of blood taken. Upon analysis, this was found to contain 0·254 gramme of urea. The convulsions continued with great violence for fifteen minutes. Coma followed, and lasted till 6 o'clock P.M., when the animal died. There was no excretion of urine after the injection of the urea. The breath was examined every hour for ammonia, but at no time was it detected; neither was it present on this day before the urea was injected. It was, however, found in the blood last drawn. There was neither vomiting nor purging.

Immediately after death, the *post-mortem* examination was commenced.

The substance of the brain appeared to be perfectly healthy; but there was considerable injection of the vessels of the meninges. The ventricles contained about 15 cubic centimetres of serous fluid. Urea was detected in this by the process mentioned, and microscopical examination. It was likewise found in the blood from the sinuses.

The vertebral canal was laid open, and the spinal cord ex-

amined. Its substance presented a normal appearance, but there was some congestion of the vessels of its membranes.

The chest contained a small quantity of serous fluid. The lungs were congested, but were otherwise healthy. The heart was of normal size, and did not appear to be in the least diseased. It contained a considerable quantity of fluid blood; 100 grammes were collected from it and the large vessels. The urea in this quantity amounted to 0·873 gramme.

Upon microscopical examination of this blood, the red corpuscles were found to present a crenated margin, and to be in decidedly less than the normal quantity. The white corpuscles were very much increased in quantity; as much as in well-marked leucocythemia.

The cavity of the peritoneum contained a small quantity of serous liquid. The membrane was in places slightly congested.

The liver was healthy in appearance, but the spleen was considerably enlarged, and contained much more than the normal quantity of blood. The tissue of this latter organ, when examined microscopically, was found to present several important deviations from the normal structure. The Malpighian corpuscles were almost entirely absent, and there was a very great increase in the number of parenchyma cells. These latter were much larger than I have ever found them in the spleen of the dog. The red blood corpuscles in the splenic blood were generally aggregated in groups, and were of irregular forms.

The stomach was opened, and presented nothing abnormal. The contents, consisting of mucus with a few pieces of bone, were of alkaline reaction, and contained both urea and ammonia; the latter in considerable amount.

The kidneys were enlarged and very much congested. Upon cutting into them, the blood poured out from innumerable orifices. There was no obstruction to either the renal arteries or veins that was discovered after death. The tissue of the kidneys, when sub-

mitted to microscopical examination, showed excessive congestion of the capillaries, and enlargement of the Malpighian bodies. Into many of these latter extravasation of blood had taken place, and the tubes were gorged with this fluid.

The bladder contained a small quantity of bloody urine.

Death in this case was, I think, obviously due to non-elimination of urea, and perhaps of the other elements of the urine, through excessive hyperæmia of the kidneys. The cause of the kidney affection I do not know. It was undoubtedly caused either directly or indirectly by the injection of the urea, for up to the time of that operation the function of these organs was perfectly effected.

The experiment cannot but be regarded as exceedingly instructive. There was complete arrest of excretion from the kidneys, and the blood, besides retaining the elements of the urine, received in addition a large quantity of urea, which remained in the organism. In many respects, therefore, the experiment resembled those in which the kidneys have been extirpated, and urea subsequently introduced into the blood. In all such experiments, death has invariably taken place within a few hours. There is, however, this important difference, that the system was saved the shock of a serious operation, and therefore one source of error was eliminated.

In relation to the alteration in the form of the blood corpuscles, it can scarcely—having Kölliker's experiments in view—be ascribed to the direct physical action of the urea, as the proportion of this substance present in the blood was altogether too small—less than 1 per cent.—to effect the change. Kölliker* found that a solution containing 30 per cent. of urea caused the red corpuscles of the frog to assume the form of stellate cells, and finally

* *Zeitschrift für wissenschaftliche Zoologie*, B. vii. s. 183; also, *Quarterly Journal of Microscopical Science*, vol. iii. 1855, p. 289.

to melt down and disappear. These alterations were also produced, though much more slowly, by solutions of 15 and 12 per cent. When weaker solutions were used, they were not caused. Human blood cells were only rendered smaller and colorless. The phenomenon observed in the case under consideration, taken in connection with the diminution of the number of red and increase in that of the white corpuscles, must probably be ascribed to some defect in the process of sanguification.

For the purpose of ascertaining the effect of introducing repeated quantities of urea into the blood, I proceeded as follows:—

Experiment. A dog, weighing forty-eight pounds, was fed as the others for three days. Ammonia was always found in the breath.

On the fourth day, at 10 o'clock A.M., 100 grammes of blood were abstracted, and, upon examination, found to contain 0·021 gramme of urea. The urine voided during the twenty-four hours amounted to 1224 cubic centimetres, and contained 8·15 grammes of urea. Ammonia was present both in the blood and expired air.

The following morning, at 10 A.M., I introduced into the jugular vein five grammes of urea, dissolved in thirty cubic centimetres of distilled water. No immediate effect was produced, the animal remaining perfectly quiet. At 11·15 convulsions ensued. One hundred grammes of blood were now taken, and yielded 0·193 gramme of urea. The convulsions, at first slight, became more violent. They continued about twenty minutes, and were succeeded by stupor. At 12 M. I injected, as before, 5 grammes of urea. Immediately afterward, the animal voided 365 cubic centimetres of urine, in which were contained 3·17 grammes of urea. The coma continued, and at 2 P.M. I again injected 5 grammes of urea into the blood. At 3·20 P.M. the dog passed 425 cubic centimetres of urine, containing 4·06 grammes of urea. The coma was still present. At 4 P.M. I injected 10

grammes of urea, dissolved in thirty-five cubic centimetres of distilled water, into the blood. The stupor was now very profound, the heart beat slowly, and the respiration was labored and stertorous. I again, at 5 P.M., abstracted 100 grammes of blood for examination. It contained 1.683 grammes of urea.

At 5.20 the dog evacuated, *per anum*, a small quantity of yellow, serous fluid. Urea and ammonia were detected in it.

At 5.45 the animal died, having in eight hours received directly into the blood twenty-five grammes of urea.

Ammonia was found in the breath during the whole course of this experiment, and likewise in the blood.

The urine voided from the commencement to the end of the experiment amounted to 890 cubic centimetres, and contained 7.23 grammes of urea. In the twenty-four hours there were evacuated 1625 cubic centimetres of urine, in which were contained 12.37 grammes of urea.

On *post-mortem* examination, the brain and spinal cord were found healthy; the membranes of both were of perfectly normal appearance. About five cubic centimetres of fluid were collected from the ventricles of the former. By simply placing a drop on a glass slide, and adding nitric acid, crystals of nitrate of urea were formed.

The lungs were found congested, but there was no effusion into the pleural cavities. The pericardium was very much congested. The heart contained a large quantity of blood. Its lining membrane, both in the auricles and ventricles, was redder than natural.

One hundred grammes of the blood from the heart and large vessels contained 1.385 grammes of urea. The blood corpuscles were of normal size and shape; but, as in the former experiments, were remarkably diminished in number, while there was an increase in the number of white corpuscles.

The peritoneal membrane was found congested in patches. The spleen was enlarged, and contained a large quantity of

blood. Beyond this the structure, when examined with the microscope, exhibited no abnormal appearance. The kidneys were healthy.

The stomach contained about one hundred and fifty cubic centimetres of fluid, resembling the rice-water discharges of cholera. The intestines also contained a quantity of the same kind of fluid. Both urea and ammonia were present in it.

For the purpose of still further determining the action of large quantities of urea, when introduced into the circulation, the following experiment was performed :—

Experiment. A small adult dog, weighing thirty and a quarter pounds, was fed as the others, for three days, on fresh meat, before any investigations were commenced. On the fourth day, at 10 o'clock A.M., one hundred grammes of blood were drawn from the jugular vein. This quantity contained 0·024 gramme of urea. The total amount of urine evacuated during the twenty-four hours was 830 cubic centimetres, containing 5·12 grammes of urea. On this and the preceding days, ammonia was always found in the breath. The food remained the same.

On the fifth day, at 10 A.M., twenty-five grammes of urea, dissolved in thirty cubic centimetres of distilled water—thus forming a nearly saturated solution—were injected into the jugular vein. The animal lay down quietly in its box, and at first did not seem to be greatly disturbed. After a few moments slight twitchings of the muscles ensued, and at 10·30 there was a strong convulsion. Some of the spasms, subsequently, were decidedly tetanic. During the convulsions, I reopened the jugular vein and allowed 100 grammes of blood to flow out. The amount of urea contained therein was 2·005 grammes. The convulsions lasted with undiminished violence till 11·10 A.M., when 481 cubic centimetres of urine, containing 7·50 grammes of urea, were excreted. They then became slighter, and at about 12 M. were succeeded by coma. This continued without intermission till

4.15 P.M., when the animal quietly died in most profound stupor. Two hundred and twenty-five cubic centimetres of urine, containing 3.12 grammes of urea, were excreted a short time before death. There was neither vomiting nor purging. Ammonia was constantly found in the breath, but not in greater quantity than during the previous days.

The blood drawn during the convulsions was examined with the microscope. The red corpuscles were altered in shape, and had become much paler than natural. Scarcely one could be found which was not more or less irregular in outline. They, besides, appeared to have lost their ordinary consistence, and when two or more came together they fused, forming an irregularly formed mass. It was thus impossible to determine microscopically their relative numbers. The white corpuscles were very much increased in quantity. The blood coagulated firmly.

The cavities of the body were opened immediately after death. The membranes of the brain were found in a state of intense congestion, and the sinuses and large vessels at the base of the cranium were gorged with blood. The substance of the brain, when cut into, exhibited a uniform pink tinge from excess of blood, and the red spots indicating the situation of capillaries were greatly increased in number. This was the first case in which the substance of the brain presented direct evidence of hyperæmia. About twenty cubic centimetres of fluid were collected from the ventricles.

The membranes of the spinal cord were likewise congested, especially in the lumbar region, though more or less throughout their whole extent. Into the cavity of the arachnoid there was an effusion of serous fluid, amounting to fifteen or twenty cubic centimetres.

The lungs were also congested, and there was a considerable amount of bloody fluid effused into the pleural cavities. The pericardium contained a quantity of liquid. The right side of

the heart was distended with blood. The left contained but a small quantity. The heart did not exhibit any indications of pre-existing disease of any kind. I was prevented examining the blood chemically. The blood corpuscles presented the same appearances as those in the blood abstracted before death.

The peritoneum was not diseased; there was no effusion. The liver was of normal appearance. The spleen was enlarged, and contained a large quantity of blood. The red corpuscles were here found almost entirely broken down into a liquid substance. No Malpighian corpuscles were discovered. Large quantities of acicular crystals were scattered through the substance of the spleen, and were visible by microscopical examination.

The kidneys were slightly congested, and some of the tubes contained blood. There were no other appearances of disease.

Two other experiments, similar to the last, were performed. As the results were almost identical, I refrain from detailed descriptions of them.

From the foregoing experiments, it is perceived that there is a limit to the power of the system to eliminate urea, and that when this substance is introduced into the blood in large quantity, it causes death by uræmia. By this I mean that the urea induces such an abnormal condition of the blood that the brain primarily, and subsequently other organs, (the kidneys included,) are brought into an abnormal condition, and are thereby prevented performing their functions. From the results of the *post-mortem* examination, it is apparent that this state is one of congestion. I am therefore disposed to think that if the brain had been able to resist the toxic power of the urea for a considerably longer period, the kidneys would have eliminated the surplus urea, and death in these latter experiments would not have ensued.

It is well known that in Bright's disease death frequently occurs from congestions and inflammations of important structures. Thus this termination may be caused by cedema of the

glottis, by pericarditis, by pneumonia, by peritonitis, by apoplexy, etc. Have we not reason to regard these several affections as due to an abnormal condition of the brain and nervous system, induced by the retention in the blood of excrementitious matters which in health are removed?

It is, I think, very evident that in neither of the foregoing experiments was there the least reason to suppose that there was any decomposition of uræa into carbonate of ammonia. In the second experiment, this substance was not found in the breath after the injection of the uræa into the blood, although it was present at two examinations before this operation.

The alterations in the blood observed with the microscope are very important, and constitute one link in the chain, connecting the retention of uræa with derangement of the brain and nervous system. They perhaps show that it is not necessary that a toxic condition of the blood should consist altogether in disturbances of the chemical balance existing between its several component parts. The morbid condition of the spleen which was found to exist is also an interesting circumstance, taken in connection with the changes in the form of the red, and alterations in the relative number of these and the white corpuscles.

Leaving, for the present, the further consideration of these experiments, I proceed to the detail of those constituting the second series, and having relation to the effects following ligature of the renal vessels, or removal of the kidneys.

Experiment. A large adult dog, weighing $68\frac{1}{4}$ pounds, was selected. At 10 A.M. the breath was examined for ammonia, and this substance was found to be exhaled from the lungs in considerable quantity. One hundred grammes of blood taken from the jugular vein contained 0.026 gramme of uræa.

At 3 P.M. the animal was placed under the influence of chloroform, and the kidneys removed, the abdomen being opened to the

smallest possible extent. Scarcely a drop of blood was lost; the anæsthesia passed off without the least untoward effect.

The next morning the dog was in apparently good condition, but manifested no desire to eat, or to move about. At 3 P.M., twenty-four hours after ablation of the kidneys, 100 grammes of blood were drawn, and found to contain 0·083 gramme of urea. The animal refused all food; ammonia was constantly in the breath.

On the third day, at 10 A.M., the dog seemed weaker. Up to this period, however, there had been no convulsion, or coma, neither was there any vomiting or purging. At about 2½ P.M. there was a slight spasm, succeeded in a few moments by a violent general convulsion. At 3 P.M. 100 grammes of blood gave 0·093 gramme of urea. At 4 P.M. the animal vomited a quantity of alkaline mucus, containing both urea and ammonia—the latter in large amount. After the vomiting, the convulsions abated in violence, but soon became as intense as at first. At intervals, however, the animal was free from spasm, and appeared to be also free from pain and uneasiness. At about 8 P.M. coma ensued, alternating with the convulsions till 10½ P.M., when it became persistent, and very profound. Death ensued at about 4 A.M. the next day, sixty-one hours after the removal of the kidneys.

The *post-mortem* examination of the body was commenced at 9 A.M. The membranes of the brain were intensely congested, and there was an effusion of about twenty-five cubic centimetres of serum into the cavity of the arachnoid. The substance of the brain, when cut into, exhibited a pinkish hue, and numerous bloody points appeared, showing enlargement, and increase in the number of capillaries. The sinuses and vessels at the base of the brain were turgid. Fifteen cubic centimetres of fluid were found in the ventricles.

The spinal cord was apparently healthy, but its membranes

were slightly congested. There was no abnormal amount of fluid found.

Both lungs were congested, and both pleuræ bore evidences of recent incipient inflammation. There was slight effusion. The heart was gorged with blood. The pericardium was healthy. One hundred grammes of blood from the heart and large vessels contained 0.097 gramme of urea.

When submitted to microscopical examination, the blood taken from the heart exhibited appearances similar to those previously noticed. The white corpuscles were increased, and the red diminished in number. These latter were also of irregular shape, and decidedly paler than natural.

The peritoneum exhibited traces of recent inflammation; a small amount of bloody serum was found in its cavity.

The spleen was very much enlarged, being at least three times the size of the organ in its normal condition, as noticed when the kidneys were removed. Upon cutting into it, the substance was found entirely disorganized, and of semi-fluid consistence. No traces of Malpighian corpuscles were to be found, and the finer trabeculæ and many of the larger were entirely detached from their connections. These, with masses of blood pigment, broken-down corpuscles, a few muscular fiber cells, and numerous acicular crystals of hæmato-crystallin, were all the morphological elements to be discovered. The parenchyma cells, white corpuscles, free nuclei, etc. had been destroyed.

The liver was also enlarged. It was not examined microscopically.

The stomach, on being opened, exhaled a strong ammoniacal odor. It contained a quantity of yellow, alkaline mucus. Ammonia was present in large quantity, and traces of urea. The intestines contained a like substance.

Experiment. At 9 o'clock A.M. 100 grammes of blood were abstracted from the jugular vein of a large dog, weighing $60\frac{1}{2}$

pounds. The urea contained therein amounted to 0.014 gramme. Ammonia was present in the breath. At 1 P.M. the renal arteries were ligated, the animal being under the influence of chloroform. As soon as the anæsthesia passed off sleep ensued, from which the dog did not awake for several hours. At 10 P.M. it appeared to be in good condition, and lapped a little milk. It was quiet, but, when spoken to, manifested undoubted signs of intelligence.

The following morning at 8 o'clock the animal was quite lively. It stood up, and even walked a few steps. It ate a little bread and milk. At 4 P.M. it was somewhat drowsy, though it could be easily roused by speaking loudly, or knocking on the side of its box. One hundred grammes of blood taken from the jugular vein contained 0.038 of urea. Ammonia was present in the breath. The stupor continued to increase, and at about 8 P.M. was profound. When last seen for the night, at 12 M., the animal was in a very comatose condition.

The next day, at 8 A.M., the coma was still present. One hundred grammes of blood contained 0.043 gramme of urea. Ammonia was exhaled from the breath, but not to a very abnormal extent. The dog remained in the same condition till about 11½ P.M., when it died, 58½ hours after the ligation of the vessels. There was no vomiting nor purging, and no visible spasms of any kind.

The following morning, at 9 A.M., I made the *post-mortem* examination. The membranes of the brain were congested, and about twenty-five cubic centimetres of fluid were effused into the cavity of the arachnoid. The substance of the brain likewise exhibited evidences of having been in a hyperæmic condition. The ventricles were distended with fluid, which, however, owing to an accident, was not measured. The sinuses and vessels at the base of the cranium were turgid with blood. The spinal cord was not examined.

The pleuræ, the lungs, the pericardium, and heart were healthy;

100 grammes of blood collected from the latter contained 0.069 of urea. Examined microscopically, the white corpuscles were found in largely increased quantity, but no other abnormal condition was discovered.

The peritoneum was congested in spots, and exhibited evidences of recent inflammatory action. The spleen was large, and softer than natural. No Malpighian corpuscles could be found. Masses of extravasated blood, in larger quantity than usual, were met with. The liver was not markedly affected. The stomach and intestines contained the residue of undigested food, with some yellow, alkaline mucus. Ammonia and urea were both present.

From the foregoing experiments, it is seen that, after the removal of the kidneys, or ligature of the renal arteries, the amount of urea in the blood was increased threefold within a short period, and that there was no reason to suppose any conversion of this principle into carbonate of ammonia. The pathological changes are interesting, and congestion and inflammation of important organs are seen to be produced as well after ablation of the kidneys, as after the direct injection of urea into the blood, or during the course of Bright's disease. The immediate cause, in each of these instances, is probably the same—derangement of nervous influence through a morbid condition of the blood.

Four other experiments, similar to the two foregoing, were performed. In all, the quantity of urea in the blood was greatly increased after removal of the kidneys, or simple ligature of their arteries, and the *post-mortem* appearances were in general the same. In three of these there were convulsions and coma, in one coma alone—as in the second experiment of this series. In one experiment, the animal lived forty-nine hours after the operation, in one fifty-three, in one sixty-eight, and in one seventy-three hours. Ammonia was found in the breath both before and after the operation. In none was there any vomiting or purging.

But that these last-mentioned results do sometimes happen,

there can be no doubt, and, in fact, judging from the investigations of these observers, they are usual concomitants. In one experiment which I performed subsequently to the above cited, they were present from the first, and doubtless by these means the urea was removed from the blood, and this fluid preserved in a comparatively normal condition. In no other way can we account for the lengthened continuance of life after the kidneys were extirpated. As this experiment is important in several respects, I give the details of it in full.

Experiment. A dog weighing thirty-eight pounds was selected for operation. Before the extirpation of the kidneys, the breath was ascertained to contain ammonia. In 100 grammes of blood were 0.009 gramme of urea.

The kidneys were removed at 9 A.M., the dog being under the influence of chloroform. After the operation, the animal fell into a quiet sleep, and did not awake for six or seven hours. At about 6 P.M. it ate a little bread and milk.

The following morning at 8 o'clock it was in apparent good condition, wagged its tail when spoken to, and ate quite freely of bread and milk. It remained in the same condition all day, manifesting, however, no desire to move out of its box, though it occasionally turned from one side to the other.

The next morning it was found that in the night a little mucus had been vomited. This contained ammonia, but no urea. No other circumstances worthy of note occurred during the day.

On the fourth day, at 7 A.M., the animal seemed somewhat uneasy from nausea. Several efforts to vomit occurred, but nothing was ejected. At about 4 P.M. there was a fecal evacuation of a thin, serous fluid of a yellow color. Ammonia was present, but no urea. Crystals of ammonio-magnesian phosphate in large quantities were visible by the microscope. No food was taken on this day.

At 7 o'clock the following morning, it was found that there

had been both vomiting and purging of ammoniacal matter during the night. One hundred grammes of blood were abstracted at 9 A.M., and found to contain 0.011 gramme of urea.

On the sixth day, there were both vomiting and purging. The animal was sensible, but refused food.

On the seventh, eighth, and ninth days, vomiting and purging occurred several times. Ammonia and urea were present in each evacuation. On each of these days, a pint of milk was conveyed to the stomach through a tube.

On the tenth day, at about 12½ P.M., a slight convulsion occurred. A pint of milk was injected into the stomach. There was neither vomiting nor purging.

On the eleventh day, at 9½ A.M., another convulsion took place, more violent than the first. The animal was, however, still sensible.

On the twelfth day, at 7 A.M., the dog was found in a comatose condition. One hundred grammes of blood were abstracted at 12 M. This quantity contained 0.041 gramme of urea. The wound in the abdomen had nearly healed. The ligatures on the renal vessels came away. Coma was present during the whole day, and death took place some time in the night after 11 o'clock. The animal was cold the following morning at 7 o'clock.

Thus life had remained for at least 278 hours after the kidneys were extirpated.

Ammonia was detected in the breath on every day but the last.

The *post-mortem* examination was commenced at about 11 o'clock A.M. The membranes of the brain were apparently healthy, but there was slight sub-arachnoidal effusion. The substance of the brain was of normal appearance. The spinal cord and its membranes were healthy. The lungs were congested, and there were several recent pleuritic adhesions. The pericardium was in several places adherent to the heart. This latter organ was in a state of incipient fatty degeneration. It was full of un-

coagulated blood, 100 grammes of which contained 0·046 gramme of urea.

The red corpuscles, both in this blood and in that abstracted on the day of death, were very much diminished in number, while the white corpuscles were correspondingly increased. The former were also broken down, and softer than is normally the case.

The peritoneal membrane was congested, and several intestinal adhesions had taken place. The spleen was enlarged, and felt like a bag of water. When the enveloping membranes were cut, the substance flowed out, like molasses in color and consistence. Examined microscopically, nothing was perceived but shreds of white fibrous tissue, masses of decomposed blood corpuscles, blood pigment, and large quantities of acicular crystals. The liver was enlarged, and in a state of congestion. The stomach and intestines contained nothing but a little mucus.

It is seen from this experiment that so long as vomiting and purging continued, there was no accumulation of urea in the blood, and no consequent uræmic intoxication. It was only when these ceased that the latter event ensued. It is therefore strongly confirmatory of the conclusion arrived at by MM. Bernard and Barreswil, which has been previously referred to. The connection between the retention of urea in the system and the occurrence of uræmia is so well marked, that it is difficult to deny to these events the relation of cause and effect.

In the third and last series of experiments, the kidneys were removed, and urea or urine subsequently directly introduced into the blood.

Experiment. From the jugular vein of a medium sized dog 100 grammes of blood were abstracted at 10 o'clock A.M., and found to contain 0·021 gramme of urea. Ammonia was detected in the expired air. At 11 A.M. the animal was placed under the influence of chloroform, and the kidneys removed. At 12 M. five grammes of urea, dissolved in thirty cubic centimetres of dis-

tilled water, were injected into the jugular vein. No immediately noticeable effect was produced. At $1\frac{1}{2}$ o'clock P.M. convulsions of great violence suddenly ensued. One hundred grammes of blood from the jugular vein yielded 0.042 gramme of urea. A large quantity of highly ammoniacal fluid was vomited. It contained urea. The convulsions continued with undiminished violence till about five o'clock, when coma gradually ensued, and remained present till death, which occurred at about 8 o'clock P.M.

Before death, and during the height of the convulsions and coma, the breath was examined for ammonia, which, although constantly found, was not present in larger quantity than before the kidneys were removed.

At $7\frac{1}{2}$ o'clock the following morning, the *post-mortem* examination was commenced.

The membranes and substance of the brain were healthy, but there was a little sub-arachnoidal and ventricular effusion.

The lungs were highly congested, as were also the pleuræ in several places. The pericardium was healthy, and the heart was of normal appearance. It contained a small quantity of uncoagulated blood. One hundred grammes taken from it and the large vessels yielded 0.032 gramme of urea.

The peritoneum was anteriorly much congested, and there was about one hundred cubic centimetres of bloody serum in its cavity. The spleen was hyperæmic, and its normal structure disorganized, as in the previous experiments. The liver was not perceptibly diseased.

The stomach and intestines contained a small quantity of alkaline fluid. It was highly ammoniacal. Urea was not detected in it.

Three other experiments, similar to the foregoing, were performed. The results were almost identical, and it is therefore perhaps unnecessary to refer to them more in detail.

In the two following experiments, urine was introduced into the blood:—

Experiment. A dog weighing somewhat less than forty pounds was used for this experiment. The breath examined for ammonia gave distinct evidence of containing it. Previous to removing the kidneys, it was determined that 100 grammes of blood from the jugular vein contained 0·017 gramme of urea.

Anæsthesia was induced by chloroform, and the kidneys extirpated at 9 o'clock A.M. As soon as the insensibility had passed off, one hundred cubic centimetres of fresh urine—voided during the induction of the anæsthesia—unfiltered, were injected carefully into the jugular vein. No immediate effect was produced. At 12 M. thirty cubic centimetres more of the same urine were introduced into the blood. The animal remained quiet in its box until about 2 o'clock P.M., when a slight convulsion ensued, lasting only a few seconds, and confined to the anterior muscles of the body. Shortly afterward another occurred more violent than the first. This was followed by others. At about 4 P.M. they ceased, and coma commenced to make its appearance. One hundred grammes of blood from the jugular vein were found to contain 0·030 gramme of urea. The coma continued till after 12 P.M. The dog was found dead the ensuing morning at 5 o'clock. There had been neither vomiting nor purging. Before death, the breath was frequently examined for ammonia, and always with affirmative results.

The *post-mortem* examination was made at 8½ o'clock A.M. The appearances observed were not materially different from those noticed in the case just detailed, except that the pericardium was congested, and there was some little effusion into its cavity; 100 grammes of blood from the heart and large vessels contained 0·036 gramme of urea.

Experiment. A dog, weighing $49\frac{3}{4}$ pounds, was the subject of this experiment. Ammonia was found in the expired air; 100

grammes of blood from the jugular vein gave 0·027 gramme of urea. The animal was at 10 A.M. brought under the influence of chloroform, and while anaesthesia was present, the kidneys were extirpated. When insensibility had passed off, 100 cubic centimetres of filtered urine—evacuated during the process of inducing anaesthesia—were injected into the jugular vein.

After the expiration of about two hours, convulsions ensued. These at first were slight, but more violent ones soon followed. They lasted till a few minutes before 3 P.M., when coma supervened; 100 grammes of blood taken from the jugular vein were found to contain 0·035 gramme of urea. The coma persisted, and at 8½ P.M. the animal died. There was no vomiting nor purging. Ammonia was found in the breath throughout.

The *post-mortem* appearances were not essentially different from those observed in the preceding experiment. The contents of the stomach were, however, acid, and did not contain ammonia.

From the experiments constituting this last series, it is clearly seen that the introduction of urea or filtered or unfiltered urine into the circulation of animals deprived of their kidneys, induces death more speedily than if such substances had not been thrown into the blood; for we have perceived from the experiments of the immediately preceding series that animals, the kidneys of which have been extirpated, or the renal arteries ligated, live for from forty-nine to two hundred and seventy-eight hours after the operation; whereas in the series last detailed, death occurred in from eight to fifteen hours, in a condition of system not to be distinguished from that known as uræmia. Taken, therefore, in connection with the experiments of the first series, in which urea was introduced into the blood of sound animals, and with those of the second, in which, through extirpation of the kidneys, the elements of the urine were retained in the blood, and we have almost demonstrative proof that the resulting uræmia was directly due to the operation of these causes.

Taken as a whole, from an attentive consideration of the foregoing investigations, I think the following conclusions are legitimately deducible:—

1st. That the injection of urea, in limited quantity, into the blood of animals, produces a certain amount of disturbance in the nervous system, similar in its symptoms to the first stages of uræmia; but that this condition even disappears if the kidneys are capable of so depurating the blood as to eliminate the toxic substance.

2d. That urea, when introduced into the circulation in larger quantity than can in a limited period be excreted by the kidneys, induces death by uræmia.

3d. That by ligature of the renal arteries, or removal of the kidneys, the elements of the urine being retained in the blood, render this fluid unsuitable to the requirements of the organism, and, consequently, induce a condition of system not essentially distinguishable from the uræmic intoxication of Bright's disease, or that caused by the direct introduction of urea into the blood. As, however, was pointed out by Bernard and Barreswil, so long as the urea, or the products of its metamorphosis, are discharged by the stomach or intestines, uræmia does not take place, but, that when these channels become closed, convulsions and coma are produced, and death soon follows.

4th. That the introduction of urea or urine into the circulation of animals, the kidneys of which have been ablated, shortens the life of such animals, as Frerichs and others have already shown.

5th. That there is reason to believe that the urine, as a whole, is more poisonous than a simple solution of urea; for in those cases in which urine was injected into the blood, the amount of urea thus introduced was much smaller than that previously thrown in, in a pure state, and yet symptoms of as great intensity followed.

6th. That urea, or the elements of the urine, as a whole, induce

such a condition of the nervous system as strongly to predispose to congestion and inflammation of the viscera, especially the lungs, pericardium, and spleen.

7th. That urea, when directly injected into the blood, or suffered to accumulate in this fluid by extirpation of the kidneys, deranges, in some manner, the process of sanguification, so as to disturb the normal relation of proportion existing between the white and the red corpuscles, and either to hasten the decomposition of these latter, or to interfere with the due removal from the blood of such as are broken down and effete.

8th. That there is no reason to suppose that, under the circumstances specified, urea undergoes conversion into carbonate of ammonia, but that, on the contrary, there is sufficient evidence to warrant the conclusion that no such process ensues. The fact that in the foregoing experiments a larger amount of urea was generally found in the blood taken from the body after death, than in that abstracted during life, is of itself conclusive against any such hypothesis.

THE END.

